THE YEAR BOOK *of* DERMATOLOGY *and* SYPHILOLOGY

(1958-1959 YEAR BOOK *Series*)

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INTRODUCTIO

It is both fascinating and gratifying to contemplate the remendous progress which has been made in dermatologic management n the past 20 years. Th s came about w th the ntroduction of the antibacterial antib otics antihi tamines orticosteroid and the antimalarials, to mention nothing of he many other minor advances in therapy The single most striking recent adva ce is the advent of griseofulvin, an oral antibiot specifically effective against certain superficial n gous infections of the sk n, hair and nails It is too early to make a definitive statement regarding the therapeutic value f this drug the safet of its prolonged administration hether or not som pecies or strains of fungi will develop es tance to it and many other pertinent but unresolved problem E en if gr seoful in should not live up to all of the resent e pectations the fact still remains that another ma or breakthrough in dermatologic therapy has been made. Furthermor it appears l'kely that when investigators go to work on the griseofulvin molecule they will undoubtedly com up w th new interesting and perhaps preferable compounds

Triam nolone acetonide preparations for topical use are among the othe noteworthy developments n dermatologic therap In many cases these appear to be uperior to the hydrocortisone preparation and they do not cause the u desir bl temic action bserved after topical application of 9-alpha fluor hydrocort sone It remains to be seen whether m h higher ncentrations of triamcinolone aceto ide topi all applied will benefit derm t ses wh h h thert ha e not been amen bl t t pical hydrocort son therap Of great int t fa th dd tional e dence ccum lated n upport f the la m that orally adm tered triamcinolone is m ffect n pso ia than th other hitherto available rtison nalogues Th not only of practical importance but of g eat theoretical nterest ince t now appea s p ble that other rtison anal gues will be developed in the f ture w th a relati ly greater (perhaps even almost pec fic t t gam t ertain dermatoses n I erta n

diseases other than those affecting the skin. This possibility should be kept in mind while engaged in therapeutic trials with new corticosteroid compounds since unless newly developed corticosteroids are given a trial in *all* important diseases which respond to corticosteroids such a "specific" effect could well be overlooked

The immunologic aspects of systemic lupus erythematosus have continued to attract much attention Certain hydantoin derivatives have been found to produce a lupus erythematosus like syndrome similar to that caused by apresoline It is noteworthy that while the clinical changes and the L.E. cell phenomenon generally were reversible in these cases the L.E cell phenomenon seemed to persist in one case although the clinical manifestations disappeared

Much has been written during the past year about the subcorneal pustular eruption described by Sneddon and Wilkinson and about other pustular and "aphthous" dermatoses The older morphologic concepts of pemphigus senile pemphigoid Senear Usher pemphigus dermatitis herpetiformis, bullous erythema multiforme pustular bacterid etc. have been discussed in the dermatologic literature for many years and newer ones such as subcorneal pustular eruptions have been described from time to time However not a single significant advance has been made in understanding the basic mechanisms underlying any of these bullous vesicular and pustular dermatoses.

Among the many reports of investigative studies included in this YEAR BOOK are those dealing with the epidemiology of plantar warts Especially instructive is the thorough and voluminous Danish work of which unfortunately only a brief summary could be presented Other investigations of special interest deal with protective measures against roentgen radiation for patient and operator and with studies on hair growth particularly the effects of roentgen ray and a folic acid antagonist on the hair root

Drug eruptions have always been among the most intriguing cutaneous diseases and dermatologists more than any other single group of physicians have contributed regularly to the knowledge of reactions to drugs and of the mechanisms producing them Particularly instructive examples this year

are eruptions due to pen cillin in milk and due to silk in vac cines.

In summary it can be said that another year has passed in which there have again been many worthwhile developments in dermatology

THE EDITORS

SELECTED BENIGN PIGMENTED CUTANEOUS LESIONS

A Discussion of Various Aspects of Their Management

By RUDOLF L. BAER *and* VICTOR H. WITTEN

Probably everyone at some time or another in his life becomes suspicious that one or more of his cutaneous lesions might be malignant. After all it is not unusual for patient and physician alike to be concerned about the pigmented spot which after remaining the same for years recently or suddenly has shown a change in size color or consistency or to be disturbed about the rough or scaly or horny lesion on the face or forehead which only recently appeared or seems to have increased in size or changed in feel or color or to express concern about the newly developed unusually persistent pimple" which he suspects may be malignant or for the parent to question the physician regarding the pigmented hairy or other mole present on his child. Among the many questions asked by the patient of his general practitioner or specialist at one time or another some of the most frequent ones are likely to be What is this little brown spot?' Is this malignant or can it become malignant?" "Does anything have to be done about this lesion? "If not, can anything be done about it for cosmetic reasons?' etc.

This has held true especially in recent years when the attention of the populace in some countries has been directed to various growths or other lesions on the skin as a result of the widespread cancer alert publicity *Many people now have* been educated to be on the lookout for newly appearing skin growths or for changes in color size configuration or feel which have taken place in lesions which may have been present for many year The majority of persons at least among our patients have thus become quite cancer conscious and consult their physician about particular cutaneous lesion to learn whether or not they need to be treated or left alone

The responsibility of the physician confronted with such problems is a definite one from the diagnostic therapeutic

From the Department of Dermatology and Syphilology (Dr M rion B Sulzberger Chairman), New York University Post Graduate Medical School and the Skin and C er Unit of University Hospital.

and psychologic viewpoints. Patients who inquire about cu taneous lesions usually do so because of real concern about their potential serion ness—not just because of morbid curi osity Therefore, it is necessary that the physician whose unsel is sought be able to differentiate between malignant and benign growths and between premalignant lesions and those known to remain benign, in o der that he can decide whether the lesion should be remo ed or left alone Of ourse it is always advantageous when a *definite* diagnosis a be made from the practical viewpoint, however insofar the lesion under discussion are concerned, this is not al way ecessary in order to adequately advise the patient.

H wever if the physician is unable to make these impor tant diagnostic differentiations, he should seek the advice of th dermatologist who i especially trained and experienced in handling these problems. In most instances the dermatol-ogi t is capable of making the diagnosis clinically and of sug ge ting r carrying out that procedure which is best suited for the treatment of the part cular lesion in the particular pa t ent Hi tra n ng and experience enable him to choose from the arious forms of available therapy and his approach is not restricted t any n routine, whether it be surgery radia tion or something lse. Where there is doubt concerning the l gnosi of a part cular lesion the dermatologist knows when how and what diagnostic procedures to carry out. Whil thos who are not specialists in dermatology cannot be pected t be familiar with all the *diagnostic criteria* and ther knowledge necessary to manage properly the many be-ign and malignant cutaneous lesions, it is their responsibil t t see that a proper plan of management is decided on—whether t be to treat the le ion or to leave it alone.

Diff ent physicia may well decide on different ways of proceedi g on one and the same lesion in one and the same pat ent Wh le th re ought to be nd there often much lati tude concerning th final decision as to therapy we feel trongly that the routine use of any *one* modality such as either rgical ex ision or radiation to manage each and ery cutaneous lesion s impractical and undes rable be ca se it i not lways in the best nterest of the patient.

I r l cu ion, we ha e elected a f w of the most common ben gn p gmented cut neou lesions which seem to us to be of

particular interest. These are *ephelis lentigo blue nevus intra dermal nevus compound nevus junction nevus* and *juvenile melanoma* It is probably safe to say that with the exception of the blue nevus and juvenile melanoma these lesions are so common that they appear on most persons during some period of their lives

HISTORY AND PHYSICAL EXAMINATION

When taking a history and making a physical examination some judgment must be used concerning the details which should be recorded. It is hardly necessary to exert the same time and effort recording information about an ephelis as about a *juvenile melanoma Detailed recording can be fa*cilitated readily by using printed outlines of the principal routine questions and rubber stamps of the particular anatomic area, for example face extremities trunk hands feet etc

Often the physical examination alone is sufficient to establish the diagnosis at other times the history is of utmost importance as previously stated For example a history of injury with an indelible or lead pencil will help to differentiate between the resulting pigmented spot and a blue nevus or other pigmented lesion the history of an injury to a site with a resulting resolving firm nodule (e g deep hematoma) or the presence of similar but more characteristic lesions elsewhere on the body may help establish the diagnosis for the particular lesion in question

History

It is wise to listen to what the patient ha to tell regarding the particular lesion or lesions about which he is concerned A knowledge of how the lesion came to the patient s attention the reasons for his worry or concern often are important aid for proper management and sometimes are helpful in establishing the diagnosis For example the patient previously may have had similar lesion which had been treated on the advice of another physician or a friend may have had a similar lesion which was left unattended and eventually was found to be malignant. Making a definitive diagno is of the presenting dermato is without first taking a history may

be a useful device for teaching morphologic diagnosis to the student of dermatology but is, in our opinion, not usually the ad isable way of proceeding for the practicing physician

In addition to whatever information the patient volun teers for medical and legal reasons it is advisable to enter the answers to the following questions about the presenting lesion in the patient s chart

1 When was it first noted?
2. What called it to your attention
3. What d d it look like when first noted?
4 Has it ncreased in size or consistency (feel)?
5 Has it changed in color?
6. Ha it developed sensory changes (itching burning ti ging)?
7 Has it ever bled?
8 H part of it come off from time to time?
9 Is it subject to irritation? What type? How often?
10. Have similar les ons been noted in the past, and if so, how were they treated?

Physical Examination

All lesion hould be examined carefully preferably in good dayl ght Where this light is not available, a lamp pro iding good blue-white light such as an ordinary gooseneck lamp with a mall shiny metal reflector containing a frosted incandescent o blue bulb can be used. A hand magnifying gl frequently is helpful in revealing the finer details of the lesion, p gmentation telangiectasia, etc. Diascopy removes the scular erythematous component and thus permits bet ter ualiz tion of the remaining features of the lesion. S m la ly gentle but firm pressure exerted with the finger tips on both les of the le ion with stretching of the skin lateral ly reduces the ascularity of the lesion and makes more obvi u it solid papular or nod lar features Among the deta ls f the lesion which we are in the habit of recording are

1 Mea urement of the horizontal and ertical axi and of ther defi t c nt urs.
2. Mea urement of the height wherever possibl a m cro-meter cal per m be used for thi purpose
3 Di tribution f color and pigment f any

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All lesions should be examined carefully preferably in good daylight. Where this light is not available a lamp pro id ng good blue-white light such as an ordinary gooseneck lamp with a small shiny metal reflector containing a frosted ncandescent or blue bulb can be used. A hand magnifying glass freq ently helpful in revealing the finer details of the lesion pigmentation, telangiectasia, etc. Diascopy removes the ascular erythematous component and thus permits better visualization of the rema ning features of the lesion. Similarly gentle but firm pressure exerted with the finger t ps on both des of the lesion with stretching of the skin lateral ly red es th scul rity of the lesion and makes more obvi u its solid papula or nodular features. Among the details of the lesion which we are in the habit of recording are

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2 Mea rement of the height where er possible a micro-vernee cal per may be used for this purpose.

3. Distr bution of color and pigment, f ny

4 If the lesion is irregular in outline a drawing of the shape of the lesion when this presents difficulties cellophane or other translucent material may be used for making an accurate drawing

5 Description of the surrounding skin (for example the presence of a dermatitis actinic changes x ray sequelae etc.)

6 The location of the lesion in relation to other structures such as the eye nose mouth ear urethral opening anus breast etc

7 In many cases a photograph of the lesion is the best record of location shape color etc

It is obvious that for certain lesions it is essential that one examine also the surrounding tissues and the related structures and for others that one examine the patient s entire body

If a diagnosis can be made with the information at hand and from the physical examination and history then appropriate therapy can be decided on at the time On the other hand where the diagnosis is not certain one can proceed in one of several ways One of these is to ask the patient to return *after an appropriate interval so that the le ion may be* re-examined for possible changes Such action would be necessary for example when the changes at first are so minimal as to preclude a definite diagnosis or where there is injury of a lesion with erythema and swelling or hemorrhagic pigmentation etc Where infection or inflammation obscure the clinical features an appropriate medicament should be applied until the lesion is re-examined a few days later

However when the diagnosis cannot be made based on the history and clinical characteristics of the lesion and where it is considered necessary or desirable to establish a definite diagnosis as quickly as possible, a biopsy of the lesion should be performed Examples are where the clinical examination does not permit *differentiation between a pigmented nevus* and a pigmented basal cell epithelioma or a junction nevus and a malignant melanoma.

Ordinarily there is no reason for the complete removal or destruction at the time of biopsy of most of the lesions discussed in this article unless particular circumstances make it advisable to do so Among these are change in size of the lesion in particular where the growth in children has been

greater than that which would be considered to be proportional with the body growth change in configuration change in pigmentation including loss or increase of pigment or change in color bleeding ulceration continued trauma that might produce inflammation or infection such as cutting with a razor blade irritation from a particular garment, etc. However since most of the lesions under discussion here are relatively small they usually can be excised completely with ease. In that event, the entire specimen can be submitted for histopathologic examination Exceptions might be larger lesions where if the diagnosis is in question only a small portion need be taken for histopathologic examination and the remainder can be destroyed at the same time by the method of choice Complete removal at the time of biopsy however is obviously indicated for certain lesions, such as a junction nevus (to be discussed later) Cosmetic considerations are another reason for complete removal in many cases.

INDICATIONS AND CONTRAINDICATIONS TO PERFORMING A BIOPSY

While there is no definite set of rules as to when and when not to perform a biopsy of a presenting lesion there are certain considerations which might be kept in mind when trying to make this decision.

A biopsy of the presenting lesion should be made when

1 The diagnosis is in question and one of the differential diagnostic possibilities if found to be correct would necessitate removal of the entire lesion or other careful attention. The histopathologic findings of most of the lesions under consideration in this article are ordinarily sufficiently characteristic to permit establishing a definitive diagnosis.

2 The knowledge of the histopathology would be of value in the over-all management of the lesion. There are times when the physician, though he is certain of the clinical diagnosis, still feels there is reason to have the tissue histopathologically examined For example where there are numerous lesions on the patient which have approximately the same clinical appearance it may be worthwhile having a histopathologic diagnosis for reference and for the record. Further

more occasionally patients are not satisfied with a clinical diagnosis and are desirous of knowing the diagnosis as ascertained by histopathologic examination This may apply in anxious and neurotic persons such as the patient who is deeply concerned about his own lesion because a similar lesion in a friend recently was found to be malignant

3 The extent to which therapy is necessary is in question Ordinarily therapy of the lesions discussed here presents no problem However histopathologic *examination of the le*sion may aid in arriving at a decision concerning the depth and width to which excision or destruction should be carried out.

4 Often when a lesion which had remained quiescent for months or years is observed to undergo change.

5 For the record Next to establishing the diagnosis performing a biopsy in order to have the microscopically established diagnosis for the record is most important In addition to the reasons already stated this applies where the patient charges or implies possible mismanagement by the physician who previously rendered treatment or where other medicolegal complications are in the offing Examples are where trauma or occupational factors etc preceded the development of the lesion or its change or where one s diagnosis differs substantially from that previously rendered.

The nondermatologist practitioner who is not certain of his clinical acumen should lean over backward in favor of histopathologic confirmation of his clinical diagnosis Often *the lesion is small and it is simpler to excise it entirely thus* completing the treatment in one session *In such instances* the physician may often decide to have a histopathologic examination done as long as the specimen is available, even though he would not have undertaken the procedure solely to obtain a biopsy specimen

Sometimes there is concern about the cosmetic result which may follow an excision biopsy Under circumstances where the location of the particular lesion or the vocation or avocation of the patient militate against any procedure which may leave more than a minimal and easily covered scar taking a biopsy should be dispensed with unless it is absolutely necessary Obviously in such cases the least destructive procedure which suffices to achieve the desired result

should be carried out Also when there is evidence that th patient has a tendency to keloid or hypertrophic scar f rma tion t s best not to take a biopsy unless thi is absolutel necessary

It is generall taught and accepted that scalpel ci n biopsy or any other type of biopsy should not be done when malignant melanoma is suspected In th regard, it i well t give consideration to stati tics from the dermatology serv ices of two well known medical schools [2] which show ed that less than 50% of the lesions diagnosed cl nically a ma lignant melanoma pro ed to be malignant melanoma on h topathologic examination. We suspect that if the error i f uch a magn tude in some dermatologic departments it i likely to be considerably greater in nondermatologic services.

It is now widespread practice to excise widely and deepl any lesion strongly suspected on clinical grounds of being a malignant melanoma Thu there i a possib lity that where maligna t melanoma is diagnosed on the basis of clinical ex mination alone (i.e where biopsy is not permitted) *in ap pr ximately 50% of the cases lesions which are not malignant mela oma might be subjected to nnecessarily extensive and perhap even mutilat ng su gery*

In the Oncology Section of ou own department howe er dermatologists who are well versed in the clinical character tic of malignant melanoma and other lesions make the correct clinical diagnosis of malignant melanoma in at least 80 of the cases. Obviously where malignant melanoma i trongly suspected on clinical grounds, the patient should ha e the benefit of the opi ion of a well-trained dermatolo gi t In this way some of the unnecessary extensive surgery wh h s done on lesions erro eously diagnosed as mal gnant m lanoma may well be avoided. When the clinically well trained specialist cannot come to a decision excision of the entire lesion without radical measures would be our proce dure of choice. However we believe that considerat on should be given to the use of this diagnostic technic when done with the cutting current (to seal off avenues of dissemination) and fter adequate x-irradiation, procedures already used in som departments,[3]

No discussion of th benign pigmented les ons of the sk n would be complete witho t a résumé of certain fundamental

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ultraviolet light in vivo By way of explanation exposure of intact living skin to ultraviolet light brings about a direct photochemical oxidation of tyrosinase which is then present in adequate quantities to catalyze the enzymatic oxidation of tyrosine to melanin. Flesch and Rothman[19] expressed the view that the sulfhydryl groups inhibited the tyrosinase by combining with copper a metal necessary for the enzymatic process. Further it has been speculated that the ultraviolet light might decrease the concentration of the naturally oc curring sulfhydryl groups, thus leaving free the copper nec essary for the complete enzymatic process.

In 1952, Fitzpatrick[1] demonstrated the presence of an in hibited tyrosinase system in nonirradiated human kin, pig mented moles ephelides lentigines and verrucae seniles. Ir radiated normal skin and malignant melanoma cells howed an active tyrosine-tyrosinase system indicating the ability of the tyrosinase within the melanocyte to convert tyros ne to m l in Intradermal and junction nevi were hown to possess negati e or weakly positive tyrosinase reaction The mechanism by wh ch the tyrosinase system s act vated by radiant energy (ultraviolet light, thorium X x rays) re ma ns to be hown.

As an additional means of demonstrating those melanocytes which contain active tyrosinase, Fitzpatrick and Kuki ta[12] used C[1] labeled tyrosine. When tissue specimens were cubated with C[1] labeled tyrosine the presence of an acti e tyrosinase system resulted in the conversion of the soluble t rosine to insoluble melanin when the unconverted water sol ble C[1] labeled tyrosine was washed away there remained the nonsoluble C[1] labeled melan n. This radioactiv ty was demonstrated by autoradiography

As wo ld be expected the fact that C[1] -labeled tyrosine is onverted to C[1] labeled melanin in the presence of an active tyrosinase ystem (as was shown to occur fo malignant melanoma) was used as a means for studying the malignancy of selected pigmented tumors. Jaeger Lerch and Delacretaz used a Geiger counter to measure the amount of C[1] labeled melan n in th tumor tissues cubated n a radioacti e tyro- si tyrosinase sy tem. They found no tyrosinase act vity in pigmented cellular nev blue nevi histiocytomas pigmented seborrheic warts nd pigmented nevi. M lign nt melanomas

subjects so essential to a proper understanding of this all important segment of dermatologic diagnosis and management.

We shall therefore present a few comments on some aspects of melanin pigmentation, the melanocyte, the histogenesis and evolution of cellular nevi and on the limitations regarding correlation of clinical and pathologic features.

BIOCHEMISTRY AND HISTOCHEMISTRY OF PIGMENTATION

Any discussion of the basic processes of pigmentation of the skin must begin with the fundamental work of Bruno Bloch[5] who in 1927 first showed by histochemical methods *that the melanin pigment of the skin was formed through a* process of enzymatic oxidation.[6, 7] In a series of ingenious experiments using tissue sections incubated in a substrate of the naturally occurring amino acid 3,4 dihydroxyphenylalanine (DOPA), he demonstrated that specialized cells in the basal layer of the epidermis, then referred to as melanoblasts (now known as melanocytes*), form melanin pigment. Further, it was concluded by Bloch that the DOPA oxidase contained *in the melanocytes of human skin acted as a catalyst* in the oxidation of DOPA to melanin.

It was then shown that with the addition of plant tyrosinase *DOPA was the first product formed in the enzymatic* oxidation of tyrosinase to melanin. Raper demonstrated that insect tyrosinase possessed both tyrosinase and DOPA oxidase activity. In 1950 Fitzpatrick, Becker, Jr., Lerner and Montgomery[7] demonstrated the presence of tyrosinase activity in human skin. In view of the distinct similarities between tyrosinase and DOPA oxidase, they recommended that the term tyrosinase be used to denote the specific enzymatic activity instead of the separate terms tyrosinase and DOPA oxidase. They were able to show that in human skin tyrosinase may exist in an inactive or partially inactive state *providing the skin has not been irradiated* with ultraviolet light. Tyrosine can act as a precursor of melanin in human skin if the enzyme tyrosinase is activated by exposure to

* At the Third Conference on the Biology of [illegible] and Atypical [illegible] held in New York [illegible] 1951 [illegible] uniform nomenclature [illegible] adopted: M[illegible] [illegible] embryonic cell with the potential to produce melanin. Melano[illegible] mature cell which produces [illegible] well [illegible] contains melanin. M[illegible] [illegible] which [illegible] melanin is contained.

cidence of junction and intradermal nevi in the various gr ups is well known and the fact that it occur i important for several reasons (1) as an aid in diagnos s (?) a an indi cation that junction nevi undergo changes with increa ing age, which manifest themselves histopathologically by a dropping (Unna) of the nevus cells from the epidermo-dermal junction into the cutis to become first compound nevi (i nev which histologically show a combination of junc tion and intradermal elements) and later become pure intra dermal nevi (when junctional elements generally are no longer found a d the ne us cells are in the dermis)[8, 27]

Spitz[23] pointed out that 98% of the nevi of children tudied by her showed junctional changes, whereas these changes were noted by Allen n only 12% of the p gmented nevi of adults Similarly Stegmaier and Montgomery[28] found that 100% of th ne of children showed junctional changes whereas Montgomery and Kernohan[29] noted that only 25% did so in adults. These observations support the opinion that ju ction nevi tend to become intradermal with increasing ge

Nevi whi h ha e junctional elements, that is, the junction nevi and compound nevi, are generally accepted as being potential precursors of malignant melanoma.[22, 31] According to Van Scott, t is in the middle and late periods of adulthood when there are fewer pure junction nevi and a greater proportion of nevi with intradermal elements that the incidence of malignant melanoma is highest.

The question naturally arises as to why the incidence of malignant melanoma is exceedingly low in childhood and relatively high in adulthood when the incidence of junction nevi is so high n childhood and relatively so low in adult hood (with the transition apparently taking place in the intervening years) As Traub pointed out in his discussion to Shaffer s paper "Whoever discovers the motivat ng factor (1) n bringing about junctional activity in the fi st place (2) in explaining why t goes to its logical conclusion as an intra dermal process in some cases and is incomplete or entirely abortive in others, and (3) what makes junctional activity fortunately q te rarely go on in some cases at some tage to true malignant activity can write the concluding chapter on this fascinating subject The same problem is discussed by

showed greater tyrosinase activity and therefore increased pigment in the more malignant and progressive tumors. The count was high also in one case of ulcerated and infected prickle cell epithelioma; this they attribute possibly to some bacteria capable of metabolizing tyrosine (using it as a nitrogen source).

Becker Jr., Fitzpatrick and Montgomery[14] demonstrated that in specimens of normal, vitiliginous and albino skin the number of melanocytes was constant and concluded therefore that the lack of pigmentation must be the result of variation in the function rather than in the number of cells present.

We concur with the hopes previously expressed by others that knowledge of this difference between the enzyme systems of the cells of benign pigmented nevi and the cells of malignant melanoma may eventually contribute to the understanding of the genesis of malignant melanoma and aid in the *in vivo* diagnosis of this tumor.

HISTOGENESIS OF NEVI

Much controversy still rages regarding the histogenesis of nevus cells and in turn the cellular nevi of man. Suffice it to say that there are three theories as to their origin: (1) that they are derived from melanocytes which are of neuroectodermal origin and are derived from the neural crest[15-19]; (2) that they are derived from epidermal cells[20, 21]; (3) that they are of double origin, a theory for which Masson[22] is the major proponent; he suggested that the superficial portion originates in the "cellules claires" or melanocytes in the basal cell layer of the epidermis and that the deeper portion originates from the Schwannian nerve cells. It would seem that the concept of the neurectodermal origin has the largest group of supporters today.

THE EVOLUTION (PATHOGENESIS) OF CELLULAR NEVI

Traub and Keil[23] pointed out that pigmented nevi, with the exception of "bathing trunk" nevi, are usually not present at birth. Junction nevi are frequent in the first two decades but become less so with advancing age. Intradermal nevi are relatively less frequent in infancy but become more common in the young adolescent and in later years. This difference in

linical characteristics of these 45 pigmented lesions were of no aid i foretelling the histopathologic diagnosis.

CORRELATION OF CLINICAL AND HISTOPATHOLOGIC FEATURES

In iew of the gaps in our knowledge of the histogenesis and evolution of cellular nevi (nevus-cell nevi) it is not sur prisi g that there is much controversy and confusion about the clinical clas fication and diagnosis of pigmented nevi On the ba of what i known about the evolution of cellular ne i t best to di t ngui h between three cl nical variet es (1) ju ction nevus (2) compound nevus and (3) intrader mal e us These three arieties are f utmost cl nical impor t nce because of the relat e frequency with which they occur various age groups th e difficulties which arise in their dif ferential diagnosis and the fact that malignant melanoma ften appea to ha e t origin in junction nd compound i nd not in the i tradermal variety

Accord ng to Becker S [*] cellular nevi re macular and u ually not more than few m ll meters in diameter n the first 4 yea of l fe after 10 years half of them ha become levated and may v ry n ize up to se eral centimeters. Macular lesions a u ually co nsidered to be of more o less ecent origin while the elevated ones which may be bearing hai are usually con dered to ha e been present longer Of ourse exceptions would be the older but still flat lesions on the mucous membranes and palms and soles

As n aid in the clinical classification and recognition of these n i, as well as the others which we will discuss, the classification of pigmented lesions by Shaffer [31] which is based on cl nical criteria, is worthy of presentation and con sideration He attempted to carefully correlate the surface morphology of the various types of pigmented nevi (wh ch he prefers to call melanocytic nevi) with their histopatholog appearan e. Fo purposes of analysis he divided the lesion linically i to the f llowing categories

1 *Flat lesions* These are macular pigmented spots, plain or speckled

2 *Slightly elevated lesions.* These tand between flat and definitely elevated lesions Th y gi e the palpati g finger

*W prefer the term "nevus-cell nevus" As used here refers to these lesions which have among their histopathologic features nevus cells

Van Scott[22] who writes "If the assumption is made that intradermal nevi transitionally develop from junction nevi as available evidence would indicate then the consideration that melanomas develop *from* junction nevi at a time when such nevi undergo transition to intradermal type cannot be avoided The inferred corollary of this may be that the true precursor lesion of melanoma more specifically defined is the junction nevus in transition to the intradermal type in which there is interference with this process Further studies concerning the normal benign invasion of the dermis by epidermis nevus cells during the transition of junction nevi to intradermal nevi would seem to be helpful in a better understanding of the pathogenesis of malignant melanoma"

INCIDENCE OF PIGMENTED NEVI

The incidence of pigmented nevi differs greatly according to different authors According to Pack and Davis[23] 2.4% of 200 infants presented pigmented nevi while Kissmeyer[24] noted that they were present in 35% of newborn infants

Siemens[25] recorded an average of 30 nevi per adult person In an examination of 1 000 adult white patients Pack *et al.*[26] counted a total of 14,609 nevi or an average of 14 6 per person *No person* was free of nevi Of these 14 609 nevi 13.2% occurred on the head and neck 0 1% on the genitalia 30.2% *the upper extremities* 30 3% *on the trunk and* 17 1% on the lower extremities. Interestingly they found nevi on the palms and soles in only 5 instances or 0 034% This extremely low incidence of nevi on the palms and soles differs considerably from the report of Lerner[27] who observed that approximately 10% of college students had nevi on these areas and the more recent observations of Van Scott Reinertson and McCall[22] who found that 25% of persons examined presented at least one such lesion These authors found that pigmented nevi rarely occur on palms and soles of children as compared with people in the 2d 3d and 4th decade Forty five of these pigmented lesions were excised from 40 of the adult patients and were examined histopathologically Seven were diagnosed as lentigo 15 as junction nevi 15 as compound nevi and 1 as an intradermal nevus The remaining 7 showed only hyperpigmentation in the basal layer The

ical diagnosis was incorrect in 26%. Investigations by Becker Sr. revealed a somewhat more encouraging picture in a clinic where dermatologists and graduate students in dermatology made the clinical diagnosis of pigmented nevus. The diagnosis was confirmed histopathologically in 80% of 710 lesions, and when the microscopic diagnosis of pigmented nevus was made the clinical diagnosis had been correct in 87% of 649 lesions.

EPHELIS (FRECKLE)

Ephelides are light tan to dark brown macules which vary in size from 1 to several millimeters in diameter. They are usually multiple, varying from a few in number to hundreds or thousands, and while usually discrete they may be grouped or confluent. They are found predominantly on the exposed parts of the body as the face, shoulders and upper back, forearms and dorsum of hands; they are infrequent on the palms and soles. They are more noticeable in persons with red hair and fair complexion.

Ephelides may appear early in life, although they are usually not seen before 6-8 years of age. They usually increase in number over the years and tend to persist; some characteristically become more prominent following exposure to the sun and other causes of increased pigmentation; others fade so as to almost disappear with the absence of exposure to the sun.

Ephelides derive their color from the collection of melanin pigment in the basal cell layer in dopa negative cells; nevus cells are not seen. These lesions remain benign and need not be treated except for cosmetic reasons where desired.

Isolated lesions may be treated by local application of a solid carbon dioxide pencil shaped to the size of the lesion. The pencil is held in place with moderate pressure for 5-10 seconds. This is followed by erythema and slight edema; sometimes a vesicle forms. The treated site then becomes darker and somewhat scaly and in about 7-10 days, when the brownish crust or scale peels away, a slightly pink spot is seen which gradually takes on the color of the surrounding skin.

Ephelides should be differentiated from lentigines, flat

slight feeling of thickness and sometimes are slightly raised above the surrounding skin.

"3 *Halos* These are elevated lesions each of which is surrounded by a pigmented macular ring

4 *Verrucoid lesions* These are pigmented lesions covered with fine digitate excrescences

5 *Polypoid lesions* The surface of these lesions consists of coarse club tipped protuberances

"6 *Dome shaped lesions* These rise smoothly from the level of the surrounding skin to form a mound like elevation.

7 *Sessile lesions* These are smooth surfaced lesions arising sharply from the surrounding skin with a slightly constricted base

"8 *Pigmented papillomas (pedunculated lesions)* These are pigmented lesions attached to the skin by means of a stalk or a pedicle"

Histopathologic examination of these 8 clinical varieties led to the following inferences group 1 lesions were almost always junction nevi groups *2* and *3* were made up of compound nevi largely group 4 consisted of intradermal nevi primarily with some evidence of junctional activity groups 5 6 7 and 8 were almost consistently intradermal nevi For details of the clinical and pathologic relationships of these lesions the reader is referred to Shaffer's original articles[31, 39] We wish to stress however that the clinical diagnosis of these nevi should not be based exclusively on the findings set forth by Shaffer who was careful to caution concerning this himself We suggest that *all* the clinical features time of onset location of the lesion as well as the age of the patient etc be taken into consideration when attempting to establish the diagnosis Unless this is done the correct clinical diagnosis will often be missed Unfortunately not many studies have been reported concerning the percentage of cases in which the clinical diagnosis was corroborated by histopathologic study Those studies which have been published however reveal a somewhat frightening situation Of 561 lesions on which the clinical diagnosis of pigmented nevus was made by nondermatologists Swerdlow reported a microscopic diagnosis which showed that they *were in error* in 39% of the cases Of 454 specimens for which a histopathologic diagnosis of pigmented nevus was made the clin

ical diagnosis was incorrect in 26%. Investigations by Becker Sr.[3] revealed a somewhat more encouraging picture in a clinic where dermatologists and graduate students in dermatology made the clinical diagnosis of pigmented nevus. The diagnosis was confirmed histopathologically in 80% of 710 lesions, and where the microscopic diagnosis of pigmented nevus was made, the clinical diagnosis had been correct in 87% of 649 lesions.

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Ephelides are light tan to dark brown macules which vary in size from 1 to several millimeters in diameter. They are usually multiple, varying from a few in number to hundreds or thousands, and while usually discrete they may be grouped or confluent. They are found predominantly on the exposed parts of the body, as the face, shoulders and upper back, forearms and dorsum of hands; they are infrequent on the palms and soles. They are more noticeable in persons with red hair and fair complexion.

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Ephelides should be differentiated from lentigines, flat

junction and compound nevi and pigmented spots associated with conditions such as incontinentia pigmenti and Jeghers Peutz syndrome.

LENTIGO (LENTIGINES)

Unfortunately the term lentigo which is so frequently used has different connotations to different dermatologists to the extent that the term is proving confusing We would therefore like to review briefly some of the lesions for which the term is used. Lever[23] states that histopathologically lentigo is represented by elongation of the rete pegs which also appear club-shaped The basal cell layer show increased pigmentation and an increase in the number of clear cells The dopa reaction is positive. No "junction" components are noted Shaffer[31] however refers to lentigo as an inactive junction nevus—in other words "a potential junction nevus without evidence of junctional activity"

Becker Sr [1] used the term "lentigo maligna as follows lentigo meaning an acquired brown macule and maligna denoting the ominous nature of the process I believe that lentigo maligna is an obligative premalignant (or malignant) lesion (i e for malignant melanoma —Eds.)

We are of the opinion that in order to avoid confusion it is best to adhere to Lever s definition and use the term *lentigo or simple lentigo to apply only to the lesion clinically described below* which does *not* possess nevus cells or junctional elements

Lentigines ordinarily *are medium to dark brown* sometimes with a blackish hue and vary in size from approximately 1 millimeter to several millimeters in diameter They are macules or very slightly elevated papules and are irregularly round or oval in configuration They appear singly or in great numbers and are usually discrete and isolated They may appear anywhere *on the body surface* although they are most common on the genitalia thighs and trunk In the aged the lesions are more frequent on the dorsa of the hands the forearms and the face (lentigo senilis)

Lentigine may appear at any age *although they usually* develop early (within the first 3 years of life) ordinarily persist for years and generally remain unchanged Their [illegible]

ence i not usually influenced by exposure to the sun al though some may darken in color with prolonged exposure

Lentigines must be d fferentiated from ephelides junction and compound nevi and sometimes even early malignant melanoma. There is et another variety of lent go referred to by Cawley and Curtis[43] as *lentigo senilis* (commonly called li er spot ") These are pigmented lesions which are irreg ular n shape may reach the s ze of 1 cm or more n diameter v ry n color from ligt t to dark brown, may be present ingly or in numbers and are located primarily on the dorsa of the ha ds and wri ts and less often on the face and ankles They are quit common occurring in 25-30% of person over 50 ears f ge They rar ly become malignant. Their histologic chara teri t in lud a moderate degree of acanthosis, large ell in the stratum mucosum fairly numerous clear cells in the basal l yer which heavily pigmented and eccentric th mb-l ke bud from the rete pegs. The cells of these bu l trongly dopa positi e Zones of atroph c dermis and bas-ophilic degeneration re seen

Beca se f the benign nature of simple and senil lentigo they rd narily do not have to be removed except for diagnos ti or co metic purposes. When they are small they can be exc ed easily with a scalpel thus affording a histopathologic diagnosis and an acceptable cosmetic result. The ery light colored lesions may be destroyed either with sol d carbon d x de o by electrodesiccation and curettage.

BLUE NEVUS (JADASSOHN-TIECHE)

Th bl e evus usually dark blue, but the shades may ry from light to da k, including yellow brown gray l ght blu a d e en black The pigment, wh le usually sol d ma be mottled The lesion vary in ize from 1 to 2 mm. to 1 cm. and sometimes larger in diameter They are usually firm and mooth, slightly el vated to hemispherical and round to o al lthough th y may hav a slightly rregular configuration Blu ne usually develop during infa cy Ordinarily they main unchanged nd only one such lesion is found on any one person although th appearance of several lesions is not u ual The lesion re discrete and may be found anywhere

on the surface of the skin, the greatest number occurring on the extremities and face.

The color of the blue nevus is the result of the collections of melanin in the dendritic cells (melanocytes) in the cutis. The pigment in these cells appears blue or blue black to the eye as the result of light being refracted through the superficial cutaneous tissues; the color varies with the depth of the pigment in the cutis. The blue nevus cells are dopa positive early in life but may later lose this activity, especially in the deeper cells. The origin of these cells—whether from the sheath of Schwann (Masson) or from melanocytes interrupted in their migration from the neural crest to the basal layer of the epidermis—remains in controversy.

These lesions are benign and ordinarily need not be treated except for cosmetic reasons. Because of their small size they are best removed by simple surgical excision with a 1-2 mm border of normal skin and primary closure. In the extremely rare instances where malignancy has occurred, the lesion usually has been found to be a cellular blue nevus, i.e., a combination of blue nevus and cellular nevus. The cellular blue nevus is usually larger and more elevated than the ordinary blue nevus.

The blue nevus must be differentiated from hemangioma, glomus tumor, epithelial cysts, intradermal and junction nevi, and more often from malignant melanoma. At times tattoos prove confusing in the differential diagnosis.

INTRADERMAL NEVUS

Intradermal nevi vary in color from that of the skin to medium or dark brown. Rather than always appearing solid in color, on careful examination flecks of tan to brown pigment are sometimes seen. The lesions vary in size from 1 to 2 mm to many centimeters although they are more commonly approximately ½–1 cm in diameter. They may or may not contain hairs. These lesions are ordinarily elevated; some are only slightly elevated while others are hemispherical, sessile or pedunculated. From one to many dozen may be located anywhere on the body surface although they are most common on the face. While these lesions are rarely present at birth, they often appear later in life, most frequently during the adolescent or young adult years.

Histopathologically the intradermal nevus is characterized by true nevus cells located in the cutis and separated from the basal layer

Treatment of these ordinarily benign lesions is not necessary except when they are located in areas subject to frequent trauma or irritation or for cosmetic reasons Numerou forms of treatment may be used all of which if properly applied, afford a satisfactory cosmetic result. These *include* desiccation nd curettage superficial desiccation and curettage followed several weeks later by the local application of trichloroacetic acid, the repeated application of trichloroacetic acid alone ablation of the lesion with scalpel followed by light desiccation of the base, or ablation with scissors (by these latter methods specimen may be procured for hi topathologic study) and the repeated introduction of a fine needle and galvanic current through the base of the nevus in a cross hatched fashion. Any of these methods should be used i uch manner that the lesion is flattened down to the level of the skin without attempting complete removal.

When th ntradermal nevu is hairy it is wise to first remove th hairs by electrolysis before attempting any other method for destruction of the nevus for when the hairs are removed first, the nevus itself sometimes shrinks and therefore lea es les tissue to be destroyed. As a matter of fact, the depilation alone is sometimes sufficient to remove smaller hairy intradermal nevi and produces a most acceptable cosmetic result.

I tradermal nevi must be differentiated from junction and compound nevi which they most closely resemble and less f equentl from fibromas, cutaneous nodules, pigmented basal cell epitheliomas and seborrheic keratoses.

COMPOUND NEVUS

The term compound nevus as previously pointed out, refer to those lesions which histologically show both junction nevus cell lements and intradermally s tuated nevus cells Traub nd Keil[22] referred to th s type of lesion as combined r mi ed nevus but t would seem that through common sage it has been replaced with the term compound nevus nd that the terms combination nevus or m ed nev s

have come to mean a combination of a nevus-cell nevus with some other entirely different variety of nevus

While compound nevi clinically have some of the features of the intradermal nevus, they are usually more pigmented *may be flatter and less well defined* and thus are more likely to simulate the junction nevus. They occur prepubertally and in later years According to Allen the chances of a compound nevus becoming malignant are very low Van Scott *et al* make the point that the incidence of malignant melanoma is

INDICATIONS FOR THE TREATMENT OF NEVUS-CELL NEVI

Treatment Mandatory

1 Those which have undergone changes or shown activity such as sudden enlargement, bleeding inflammation, alteration in color (either darker or lighter) ulceration, crusting, development of satellite pigmented areas, or *those which become symptomatic (especially pruritic* or painful)
2 Those showing activity during pregnancy[43]
3 Those which histologically show evidence of unrest e g precancerous junction nevi.[44]
4 Those in which the physician recognizes clinical features which suggest the presence of one of those closely related conditions which are known to undergo malignant transformation in a high percentage of instances (e.g melanotic freckle of Hutchinson[45] and precancerous melanosis.)[46]

Treatment Generally Considered Advisable

1 Nevus cell nevi at sites where the incidence of malignant melanoma is relatively high such as genitalia, mucous membranes and subungual areas.[34]
2 *Juvenile melanomas* [28, 47]

Treatment Controversial

1 Those at sites of repeated trauma.
2 Those appearing beyond the 2d decade of life
3 Those located on palms and particularly on soles (see text)

From Witten, V H., and Kopf A W Some common misconceptions regarding nevi and skin cancers, M Clin North America (in press)

highest apparently when the proportion of nevi with intradermal elements is greatest i e in those age group where transition from junction to intradermal nevu occurs with *the greatest frequency* In view of the differing stat[...] and varying conclusion this problem requires clarification

Compound nevi may be treated by any one of several methods *provided therapy* i necessary at all (see table) Where there is any *doubt concerning the diagno[sis]* scalpel exci[s]ion with conservative borders is the treatment of choice (see Junction Nevi) where the pigment is confined t[o] the [...]um

mit of a "hemispherical lesion it may be ablated with a scal pel (thus affording a biopsy specimen) and the base desic cated and curetted. We do not favor cryotherapy escharotics or electrodesiccation of lesions suspected of being compound nevi they should be managed as abo e or left alone

JUNCTION NEVUS

In 1940 Traub and Keil while presenting a cla ification of the pigmented ne i based on the microanatomic location of the lesions, first used the term junction nevus and used the expression common mole to designate the intradermal nevus.

Ju ction nevi ary in size from approximately 1 mm. to many centimeters in diameter and in color from very light tan t dark brown (even black) It is not unusual for the pig mentation to be mottled in distribution. Ordinarily junction nevi are flat or slightly elevated are well defined and may ha e the configuration of a small papule or a large hemispherical nodule The surface of these lesions is usually smooth although it may become roughened. Hairs (other than lanugo) are usually absent. The number of lesions var es from one to several dozens. They usually occur singly anywhe on the body but in particular on the extremities and the face on the trunk, they are most commonly located on th upper ba k and shoulders.

Pigmented nevi of the palms and soles ordinarily are flat and are junction nevi. In these locations they vary in size from a barely visible fleck of pigment to light tan to dark brown areas up to 1 cm. or more in size. Careful examination of these lesions will often reveal a speckling of the pigment at times ppearing as small pseudopodia extending out into the apparently normal tissues.

J nction nevi may appea t any ag nd may increase in size ery slowly until they reach the average l mits for this particular variety of nevus. Histopathologically true nevus cells are found in theques (nests) in the basal cell layer together with clear ells in addition, nevus cells are found in the uppermost cutis at the junction of epidermis and dermis.

Ordinarily junction nevi remain ben gn, but when malig nant melanoma does develop from a previously existing ne-

vus it is usually a junction nevus or less often a compound nevus Because of this possibility great concern and caution are voiced regarding the management of these particular nevi While there are some physicians usually nondermatologists who recommend the surgical excision of *all* lesions suspected of being junction nevi there are many reasons which speak strongly against this viewpoint.

It is not unusual for patients to have been advised that such pigmented lesions be excised before puberty and early in pregnancy as the incidence of malignant transformation is apparently greater during puberty and gestation However just as it is impractical and illogical to excise all pigmented lesions suspected of being junction nevi so is it illogical to excise all those pigmented lesions present before puberty or during early pregnancy The indications for excision of pigmented lesions during these two periods of life remain the same as the indications for the removal of any of the pigmented lesions previously described

According to one group of investigators[22] ¼ of the individuals of our total population have one or more pigmented nevi on the palms and soles the greatest percentage of these lesions are junction nevi While there are some physicians who advocate surgical excision of *all* such lesions because of the possibility of their becoming malignant melanomas it is our opinion that such management is out of the question as is the removal of *all* pigmented nevi which occur elsewhere on the skin surface

Where lesions are clinically suspected of being junction nevi and when there are distinct *indications* for the removal of such lesions (see table) the treatment of choice i conservative surgical excision including about 1 or 2 mm of normal tissue at the periphery Such a procedure is carried out under local anesthesia and the wound is closed by sutures

Junction nevi must be differentiated from intradermal nevi compound nevi malignant melanomas lentigines cutaneous nodules blue nevus tattoos *cafe au lait spots* etc

BENIGN JUVENILE MELANOMA
(JUVENILE MELANOMA; PREPUBERTAL MELANOMA)

Of all the pigmented lesions occurring in young people none is more important in differential diagnosis nor more

misunderstood than the one referred to as juvenile melanoma, a term coined by Spitz. The difficulty in establishing the diagnosis of the lesion based on gross morphologic appearance is the result of there being no absolutely characteristic clinical picture. In addition the histopathologic picture of benign juvenile melanoma is often confused with that of malignant melanoma of adults. It is obvious that it is extremely important to be able to recognize benign juvenile melanoma and to differentiate it from malignant melanoma since the clinical course of benign juvenile melanoma is benign in contradistinction to malignant melanoma from which one can anticipate a high percentage of metastases and eventual death.

The very use of the word melanoma is in itself confusing as common usage has given the term the meaning of malignant melanoma and therefore interpretation by the uninitiated would lead to the erroneous conclusion that a (benign) juvenile melanoma* is a malignant melanoma occurring before the onset of puberty. As we shall attempt to point out, this is *not* the case, as there are certain clinical and histologic characteristics which help to differentiate the benign juvenile melanoma from the *malignant melanoma which in exceptional instances also may occur in prepubertal years.*

The benign juvenile melanoma is often difficult to recognize and therefore the clinical diagnosis ordinarily would not be suspected except by specially trained and experienced dermatologists or other physicians. Nevertheless the clinical features of benign juvenile melanoma may be of some help in making the diagnosis. Benign juvenile melanomas vary in color usually from pink to red although they may bear pigment from brown to black. Ordinarily by the time they are called to the physician's attention they are approximately 1 cm in size, although they may be larger. They are round or oval, occasionally have irregular borders, are sharply defined and elevated, are usually quite smooth but may be rough or verrucous at the surface. Dark, coarse hairs are not ordinarily seen.

Benign juvenile melanomas can occur on any part of the

*If further experience should confirm the benign nature of juvenile "melanoma," we would strongly urge [illegible] a name for this lesion which would not include the word "melanoma." Until such time, we prefer the term "benign juvenile melanoma" also used by Spitz and Allen as well as by McWhorter and Woolsey.

body but seemingly are more common on the face and extremities—in particular the lower extremities. They may be present at birth or develop anytime thereafter but usually within the first 3 years. They usually grow slowly and it may be difficult to decide whether the growth is in proportion with the child's growth or greater. Lesions with these clinical characteristics which also have the "accepted" histopathologic picture of benign juvenile melanoma described by Spitz and Allen as a rule remain benign. It is obvious therefore that the final diagnosis depends on the correct interpretation of the histopathologic changes.

The incidence of true malignant melanoma (melanocarcinoma) in childhood has been stated by Allen to be in the vicinity of 0.3% of all melanocarcinomas of the skin and mucous membranes. On the other hand the incidence of benign juvenile melanoma is quite high when compared with ordinary benign nevi occurring in children; according to Spitz the ratio is approximately 1:12. However, it should be taken into consideration that this ratio may well be greatly biased in favor of benign juvenile melanomas since only highly selected nevi are ordinarily removed during childhood. The ultimate outcome of untreated benign juvenile melanomas for the time being remains unknown, but when one considers *their apparently significant incidence in childhood* and the very low incidence of melanocarcinoma in childhood, then one is justified in assuming that their course is essentially a benign one during this period of life.

The incidence of benign juvenile melanomas drops sharply after puberty and they are rare after the 3d decade. It is assumed, therefore, that benign juvenile melanoma may acquire the histologic characteristics of intradermal nevi after puberty. If all the evidence which has been accumulated to date indicating the benign character of benign juvenile melanomas is correct, then *treatment need be conservative*, only consisting of surgical excision with a margin of a few millimeters. There is *no need for wide and deep radical surgery*.

It is not our intention here to set forth in detail the histopathologic criteria for the diagnosis of benign juvenile melanoma. We do, however, side with those authors who agree with the opinions of Spitz[26] and Allen[2] that the diagnosis of this melanoma can be made by *experienced* pathologists

through recognition of certain histopathologic features

The cytologic features of benign juvenile melanoma as described in 1948 by Spitz include (1) the relative superficiality of the essential landmarks of the lesion (2) the two elements of a compound nevus, junctional and intradermal (3) edema and telangiectasia of the cutis just below the epidermis (4) the tendency for single cells or compact nests of spherical or spindle cells to be segregated sharply from the adjacent ones (5) the occurrence of large cells with abundant, usually uniformly basophilic, myogenous-appearing cytoplasm (6) the superficially located characteristic giant cells, those with the single large nucleus as well as the multinucleated ones resembling the pattern either of the giant cells of measles or Touton giant cells with a complete or incomplete peripheral rim of small nuclei (7) the generally abrupt transition between the acantholytic, loose junctional cells and the still intact adjacent epidermis and (8) the relative sparsity of pigmentation, so that, in association with the superficial dermal edema and telangiectasis most of the juvenile melanomas clinically appear purplish-red rather than dark brown. In addition to this very distinctive coloration, the juvenile melanomas tend to be hairless larger and more elevated than the usual nevus of childhood.

On the basis of the histologic criteria just outlined, it is possible, in about two thirds of the cases, to learn to differentiat the benign juvenile melanomas from the adult melanocarcinomas in the remainder this histologic differentiation is not possible without knowledge of the age of the patient. However if the prepubertal age of the child is made available to the pathologist, there then can be very little doubt that the lesion is benign if the exceptional patterns outlined in the following sections are borne in mind.

There is some evidence that not only do benign juvenile melanomas become simple intradermal nevi after puberty but that a small percentage of melanocarcinomas in adults show some residual evidence of a pre-existing benign juvenile melanoma. The benign course of the benign juvenile melanoma diagnosed according to the clinical and histopathologic criteria outlined, together with the much lesser incidence of these histopathologic findings in lesions studied after puberty all point to the justification for conservati e management of

these essentially benign growths To perform *radical* surgical extirpation of every lesion having the clinical and histopathologic features of a benign juvenile melanoma would be comparable to amputating every breast with cystic mastitis simply because of the possibility that carcinoma might develop in these tissues in later years.

The practical approach then to the management of any lesion which clinically is suggestive of a benign juvenile melanoma would be simple surgical excision including only several millimeters of normal appearing surrounding skin Because of the small size of these lesions the wound usually can be closed easily by suture to heal by primary intention. This procedure then allows for accurate histologic diagnosis provided the specimen is sent to a pathologist who is especially well trained in the field of dermatologic histopathology We are stressing this fact because it has been our experience repeatedly that the same specimen which is correctly diagnosed by the specially trained dermatopathologist as a benign juvenile melanoma is often interpreted as a malignant melanoma by highly competent general pathologists The procedure of simple excision with a narrow border of normal skin also completely eliminates such lesions as a source of possible future difficulty This is of potential importance in case further studies in this field should suggest that remnants of benign juvenile melanomas later in life may become the source of true malignant melanoma.

GENERAL REMARKS REGARDING MANAGEMENT

Rather than review the various statistics indicating what percentage of malignant melanomas originate from junction or compound nevi it seems to us more important to point out that it is estimated that only one out of a million or more pigmented nevi becomes malignant [8] Considering that the average person has approximately 20 nevi this would mean that 1 person in 50 000 can be expected to develop a malignant melanoma from clinically evident pigmented lesions The phrase "clinically evident pigmented lesions" is intentionally used as apparently *a large percentage of malignant melanomas have their origin at sites clinically free of existing nevi*

As discussed elsewhere, we agree with those who feel that each nevus must be individually evaluated and that the deci sion a to whether or not t should be removed and the method to be used should be based on consideration of all fac t rs[40]

After the decision has been made to remove gi en lesions general those diagnosed as junction or compound nevi or a benign juvenile melanomas should be surgically excised w th a narrow border Elevated, dome-shaped sessile, pedun culated and polypo d lesions may often be sn pped off at the base which in turn is electrodes ccated.

Pigmented lesions such as ephel des simple lentigo senile lentigo and i tradermal nevi, as has been pointed out, may be destroyed by a number of means including the application f tri hloroacetic acid carbon dioxide pencil electrodesicca tio te When any of these methods are used for cosmetic reaso s fforts hould be made to destroy all of the areas of p gmentation. Ther are undoubtedly many hundred of tho sands and perhaps, millions f lesions some of which almost certa ly junction nevi wh ch are destroyed by n or mo e of these means every year And we know of no pr perly documented evidence wher histologic lly verified benign pigmented lesions were timulated to becom malig nant m l nomas as a esult of burning the surface cutting through the lesion or other local traumatic exercises. Of rse when the diagnosis is in question a specimen should alw ay be taken for histopathologic examination. Should the lt of microscop c tudy uggest possible malignant tra f rmation then th remaining area plus an area of normal appearing surrounding skin can be surgically excised.

A great co tro rsy has urrounded the question concern ng whether a lesion suspected of being mal gnant melanoma might be cut into for the purpose of obtaining ti sue fo mi roscopic study if such a lesion, n tially should be totally ex sed widely and deeply Wh le it is difficult to establish defin te criteria which pply in all cases we are of the opinion that where there is serious doubt that the lesion is a malig nant melanoma with rare exceptions t should be excised in toto w th llowance only for a *mall border* of clinically normal tissue Add tional surgery can always be carried out f the diagnosis of malignant melanoma is histologically con

firmed This procedure helps to avoid unnecessary cutting into the lesion as well as unnecessarily extensive surgery

A decision regarding the management of lesions which are *highly suspected* of being malignant melanoma can be made only after consideration of *all* of the factors involved and such decisions should be made only by experts in this particular field preferably a team consisting of a dermatologist and a tumor surgeon.

CONCLUSIONS

The clinical and histopathologic features of selected benign cutaneous pigmented lesions and their management have been reviewed These lesions are among the most important cutaneous problems with which the practitioner is confronted They are also among the most common particularly in recent years because of the publicity which has surrounded pigmented moles [n]

While the vast majority of these pigmented lesions remain benign, one in many millions eventually undergoes malignant changes Therefore it is essential from both the prognostic and therapeutic viewpoints that one should know which particular varieties of these lesions do and do not possess such malignant potentialities

In most instances the well trained clinician can establish a diagnosis on the basis of clinical examination and the history In doubtful cases a histologic examination preferably by a pathologist who has had special training and experience in the diagnosis of pigmented lesions is an absolute necessity Only in this manner is it feasible to avoid potentially serious mistakes

A continuing search must be carried on for biochemical or other in vivo methods which will permit differentiation between benign and premalignant or malignant pigmented lesions.

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1 TREATMENT AND PREVENTION

A. Local Drug Therapy

Treatment of Dermatoses with Local Application of Triamcinolone Acetonide, New Synthetic Corticoid. Preliminary Report is presented by Raymond C V Robinson. In a pilot study n 35 patients, u ing th double-bl nd, paired comparison method, the anti nflammatory action of 0.1% triamcinolone acetonide lot on was found to be similar to that of lotions contain ng 0 1% fludrocortisone or 1% hydrocortisone In 40 patients w th inflammatory dermatoses 0 1% triamci lone acetonide n water miscible base was at least as effect e a 1% hydrocortison n the same water miscible base

Satisfactory results were obtained in the treatment of 74 f 76 patients with topic dermat tis, 31 of 32 with seborrheic dermatitis, 38 of 40 with contact dermatit s, 17 of 17 patients with locali ed neurodermatitis, 8 of 9 with pruritu ni and 7 of 8 with pruritus ul a u ng 0 1% triamcinolone cetonide ointment or l tion. There wa no gnificant effect on psoriasis lesions As with other locally pplied corticoids, flare-ups occurred after d scontinuance of local applications of triamcinolone R l ef wa maintained howe er for the duration of treatment, and it wa usually poss bl to lessen the freq ency of appli tion s ymptom subsi led.

Six patients with Candida albicans paronychia and 16 with C alb cans nfections of the genitocrural region were treated with a cream containing 0 1% triamcinolone acetonide and 100,000 un ts of ny tatin 2 5 mg neomycin sulfate and 0 25 mg Gram cidin/Gm. 3 with paronychia and 14 with crural moniliasis were mpro ed.

Triamcinolone Acetonide Highly Effective New Topical Steroid has n anti- nflammatory effect in animals 40 times as great as cortisone or hydrocortisone. In a double-blind study J Graham Smith J Raymond J Zawiaza and Harvey Blank[2] (Univ of Miami) compared 0.1% triamcinolone ace

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1) Bull School Med Univ Maryland 43 34 37 July, 1958
2) A M A Arch Dermat 78 643-44 November 1958

tonide with 1% hydrocortisone as used topically in lotion cream and ointment bases in 109 patients with inflammatory skin diseases After treatment for 1 week to 1 month or longer each patient was asked to evaluate the preparations. The examining physician also made an evaluation of the sites of application for objective evidence of difference in effectiveness

In 75 patients (68.7 %) 0 1% triamcinolone acetonide was more effective subjectively and objectively than 1% hydrocortisone. In 27 patients the drugs were equally effective subjectively and in 28 patients were equally effective objectively In only 4 patients (3.7%) was there subjective evidence of superiority of hydrocortisone and in 3 (2.8%) objective evidence Patients who had been treated unsuccessfully with many other topical steroids showed for the first time complete regression of lesions after treatment with triamcinolone acetonide. Body weight of several patients was followed but there was no gain or loss. After extensive local use of 30 ml. of 0 1% triamcinolone acetonide daily for 6 days in 1 patient no changes occurred in chloride sodium and potassium serum electrolytes or in body weight No case of sensitivity was observed.

► [In our own experience triamcinolone acetonide is proving to be the most effective topical corticosteroid yet to be introduced We know of no reports of systemic absorption and undesirable side effect from the continued and widespread use of this compound It is particularly interesting that when given orally the acetonide no more effective than triamcinolone free alcohol —Eds]

Experimental and Clinical Evaluation of New Hydrocortisone Derivative (Hydrocortisone 21 Xanthogen Ethanolamine) for Topical Use H Haxthausen[3] (Univ of Copenhagen) observes that the hydrocortisone derivative is hydrolyzed in the presence of water It is relatively stable in a mixture of 1 part lanolin and 9 parts petrolatum but even here 20% decomposition occurs in 2 months of refrigeration

By use of the electrophoretic patch test 1 3 % hydrocortisone-21 xanthogen-ethanolamine (corresponding to 1% hydrocortisone after hydrolysis) 1% 9α fluorohydrocortisone and 1% hydrocortisone acetate were compared in 20 experiments Each substance was used in a base consisting of 1 part lanolin and 9 parts petrolatum and the base itself was

(3) Acta dermat venereol. 37 435-439 1957

used as a control. Strong to complete inhibition of the eczematous reaction resulting from electrophoresis occurred in 3 instances with hydrocortisone-21 xanthogen-ethanolamine and in 2 instances with fluorohydrocortisone. Weak to moderate inhibition occurred in 10 experiments with the new substance, 5 with hydrocortisone acetate, 9 with fluorohydrocortisone and 1 with the control. The results indicate that hydrocortisone-21 xanthogen-ethanolamine is about as effective as fluorohydrocortisone when applied topically for the purpose of inhibiting experimental eczema.

In clinical trials the new derivative was used in an ointment base made by mixing equal parts of two ointments: (1) hydrocortisone-xanthogenic acid in petrolatum and (2) ethanolamine in petrolatum 42.5%, mono-olein 2.5%, lanolin 5% and water 50%. The effectiveness of this mixture containing 1% hydrocortisone-21 xanthogen-ethanolamine was compared with that of a commercial ointment containing 1% hydrocortisone acetate in 81 cases of eczema and 38 of atopic dermatitis. The new derivative was more effective in 4 instances, hydrocortisone acetate was more effective in 12 instances and there was no difference in 66. The author concludes that the clinical effectiveness of the new preparation is somewhat greater than that of hydrocortisone acetate and is apparently about equal to that of fluorohydrocortisone. It is much less apt to produce general effects when absorbed locally, however, since it is broken down to hydrocortisone, which is much less active than fluorohydrocortisone. The problem of stability of hydrocortisone 21 xanthogen-ethanolamine has been solved by dispensing the preparation in a special double tube, the xanthogen and ethanolamine components to be mixed before application.

► [New corticosteroid compounds for topical application continue to become available. We have no personal experience with the particular compound tested by Haxthausen. Of the newer compounds which we have evaluated, triamcinolone acetonide has been the most promising. Paired comparison tests in many instances showed 0.1% concentration of this substance to be somewhat more effective than 1% hydrocortisone; 0.2% triamcinolone acetonide in turn appeared somewhat more effective than 0.1% in most cases. Whether the topical effectiveness of this compound can be augmented by increasing its concentration remained unanswered, as does the question, What is the optimal concentration from the economic viewpoint?

Perhaps the day is not far off when the pharmaceutical industry will develop corticosteroid compounds for topical application which will have

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By use of the electrophoretic patch test 1.3% hydrocortisone-21 xanthogen-ethanolamine (corresponding to 1% hydrocortisone after hydrolysis) 1% 9α fluorohydrocortisone and 1% hydrocortisone acetate were compared in 20 experiments Each substance was used in a base consisting of 1 part lanolin and 9 parts petrolatum and the base itself was

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Perhaps the day is not far off when the pharmaceutical industry will develop corticosteroid compounds for topical application which will have

different therapeutic effects on different diseases of the skin. It is entirely conceivable that one compound may prove more beneficial in the management of certain cutaneous lesions or processes while another compound may be found preferable for the treatment of others.—Eds.]

Clinical Trial. P. D. C. Kinmont[4] (Derbyshire Royal Infirm, Derby, England) discusses the planning, conduct and expression of results of a comparative clinical trial of local applications on the skin. It is essential to discuss the initial plan with the statisticians at an early stage to eliminate statistical objections. The amount of detailed information which the trial is expected to produce should be limited. If many observations are required, it is difficult to cope with more than 4 preparations at a time. The cardinal properties for agents for external use as laid down by Sulzberger and Baer are useful in assessing a local application. These are (1) high efficiency, (2) low allergenic potential, (3) very low local primary irritancy, (4) low incidence of neoplastic change after long use, (5) low systemic toxicity by absorption, (6) ease of incorporation and stability in suitable vehicles and (7) acceptability to users.

The author records the results of a controlled comparative clinical trial of a synthetic tar and of a prepared coal tar BP in a hydrocarbon base and in oil in water base. The formula for the synthetic tar was phenol and o-cresol 4.17% each, quinoline, pyridine and picoline 2.08% each, toluene 8.33%, xylene and anthracene 4.17% each, phenanthracene 16.66%, carbazole 10.43% and naphthalene 41.66%. Of this mixture 0.24% was equivalent to 1% of prepared coal tar BP. Both tar preparations were used clinically in concentration of 3% or equivalent.

A total of 603 observations made on 281 patients was subjected to statistical analysis. The synthetic tar proved more efficient, less liable to produce adverse reactions and cosmetically superior to the prepared coal tar BP. The synthetic tar was superior in eczemas of childhood, adult atopic eczema and psoriasis. There was *little evidence that one base was* superior to the other. Both preparations were stable in suitable vehicles under ordinary ranges of temperature and under normal conditions of transport and storage. The synthetic tar is of constant composition, whereas the prepared coal tar is inherently variable.

(4) A.M.A. Arch. Dermat. 77:635-641, June 1958.

► [The "improved" decolorized and synthetic coal tar preparations as well as coal tar extracts which we have had the opportunity to evaluate have never quite measured up to the therapeutic achievements of ordinary crude coal tar. However under practical conditions nonmessy tar preparations and extracts often are preferable to crude coal tar. One of the very important drawbacks to crude coal tar is the variation in chemical composition from one batch to another, this can be reflected in the differences in the therapeutic effectiveness of the different batches.

To the cardinal properties required for topical medicaments listed by the author one must add (8) lack of photodynamic and photoallergenic potential and (9) lack of immunochemical relationship to commonly encountered potent allergenic sensitizing agents.—Eds.]

Critical Evaluation of Effect of Steroid Lotions on Inflammatory Dermatoses. Ira Leo Schamberg, Samuel I. Askovitz and Marvin Greenberg[5] (Albert Einstein Med. Center) used the double-blind paired-comparison method in studying the effect of three steroid lotions and a control lotion in 510 patients with inflammatory dermatoses. A newly devised statistical method was used that utilizes the large percentage of patients in whom there was no difference in effect and which weighs the degree of difference in response to the agents studied.

1. 177 patients in whom 0.1% fludrocortisone lotion was compared with control lotion base no statistically significant difference in effect could be demonstrated. The lotion base was an oil in water emulsion containing Ceramol (a carbowax), diglycol stearate, liquid petrolatum, glycerin 6.5%, isopropyl alcohol and 0.15% methylparaben. The patients had the following diseases: atopic dermatitis, 25 patients; contact dermatitis 38; eczematous dermatitis 5; generalized erythroderma and exfoliative dermatitis 2; eczematous hand eruptions 9; hyperhidrosis and hyperhidrotic dermatitis, 1; infectious eczematous dermatitis, 1; intertrigo and intertriginous moniliasis 11; lichen simplex chronicus, 27; miliaria, 8; generalized neurodermatitis 11; nummular eczema, 10; psoriasis, 2; seborrheic dermatitis, 14; stasis dermatitis, 4 and miscellaneous inflammatory dermatoses, 9.

Analysis by age, sex, diagnosis, skin thickness and presence or absence of stratum corneum in areas of dermatitis revealed no group with significant benefit from the steroid lotion as compared with the control lotion. In 217 patients, no significant difference was found between the effect of 0.1% fludrocortisone lotion and 1% hydrocortisone lotion nor in

(5) A.M.A. Arch. Dermat. 78:490-499, October, 1958.

116 patients between the effect of 1% hydrocortisone lotion and 1% prednisolone lotion

The authors believe the following factors explain the discrepancy between the findings in this study and the experience of most dermatologists (1) It is probable that many *of the patients were placebo reactors* which explains in part not only the lack of significant superiority of the steroid over the base but also the large percentage of patients (54.8%) in whom the two were equal (2) It is difficult to evaluate the effect of drugs on disease in which a large psychosomatic factor is present. Most dermatologists agree that the psyche plays an important role in many inflammatory dermatoses (3) In the essentially unselected group of patients studied the large number of dermatoses unaffected by steroids obscured the few benefited. (4) The irritant ef*fect of the alcoholic lotion may* have overshadowed any beneficial steroid effect in many acute cases (5) Only 15 cc of lotion was available for treatment of each area. The amount may have been insufficient to bring about improvement in some patients (6) Poor penetration of the steroid through thick intact skin may have prevented demonstrable benefit in some patients. (7) Objective improvement may have oc*curred in the control area due to relief from pruritus* thus obscuring the beneficial effect of the steroid. The first three factors are probably the major ones The placebo reactor is an especially important potential source of error in studies on the effect of therapeutic agents

► [One of the difficulties in this study appears to be that a large number of the patients had eruptions which are not expected to be benefited by topically applied corticosteroid preparation A factor possibly responsible for bilateral improvement which was not considered by the authors the effect of the corticosteroid preparations on distant sites (by way of external spread?) which often has been reported In a planned study such this the patient should be carefully instructed to use different fingers when applying the two preparations to avoid contamination of the placebo-treated areas with the corticosteroid Despite these factors and the other *described by* the authors, we have not had any difficulties in demonstrating significant differences in the therapeutic effectiveness between corticosteroid and placebo preparations, as well as between different corticosteroid medications This can be achieved by using not only the paired comparison method, but by selecting patients in whom beneficial effect can be expected from the "active" medication —Ed]

Injection of Hydrocortisone into Dermatologic Lesions was carried out by Leonard E. Savitt[6] (Los Angeles) In

(6) A.M.A. Arch. Dermat. 6 738 742, December 1

most cases hydrocortisone sodium succinate (Solu-Cortef) 50 mg/ml was injected locally in weekly doses of 25-50 mg/injection for 4-8 weeks. Since pain was often produced when normal saline was used as the recommended diluent 2% procaine was substituted to lessen the pain. For comparison in some patients a suspension of hydrocortisone acetate 50 mg/ml, was used. The intralesional injections apparently had no adverse effects. Care was taken that the injection did not cause blanching. When blanching was inadvertently induced it caused a minute slough that readily healed.

Some improvement occurred in 31 of 39 patients. Raised lesions responded better than relatively flat ones. Localized lesions improved more readily than diffuse ones. Firm lesions such as keloids responded poorly. The indurated lesions of chronic discoid lupus erythematosus decreased in size whereas somewhat flat lesions did not. Lesions of sarcoidosis that responded soon relapsed.

Improvement of 75-100% occurred in 2 of 7 cases of discoid lupus erythematosus, 1 of 2 cases of localized myxedema of the legs, 1 of 2 cases of sarcoidosis, 2 of 3 cases of lichen simplex chronicus (which had failed to respond to other modalities), 3 cases of cystic acne of the neck, 2 of 3 cases of granuloma annulare, 1 of 2 lesions of necrobiosis lipoidica diabeticorum in the same patient, 6 cases of ganglions of the hands or wrists, 1 synovial cyst on the index finger, 1 case of hidradenitis suppurativa and 1 case of xanthoma tuberosum. In a patient with chondrodermatitis nodularis chronica helicis, pain disappeared after 1 injection and the lesion decreased in size 50% after 4 injections. Three patients with keloid responded poorly but there was no recurrence in 1 case in which excision was followed by injection of hydrocortisone. No improvement occurred in 2 cases of granuloma of the axillae caused by deodorant and 1 case of foreign body granuloma. Improvement was about 50% with repeated injections in a case of vitiligo. Pruritus in a case of lichen planus of the vulva was relieved.

Hydrocortisone acetate is more useful than hydrocortisone sodium succinate for intralesional use, because the latter causes more pain on injection and must be used within 24 hours after dilution.

► [Intralesional injections of suspensions of hydrocortisone and other cor

ticosteroids deserve a trial in selected cases of alopecia areata, lichen simplex chronicus, hypertrophic lichen planus, necrobiosis lipoidica (see following abstract), cystic acne and other circumscribed dermatoses. Apparently the insoluble preparations generally do better than the soluble ones. Atrophy of the skin is the most disagreeable side effect this atrophy varies considerably in degree and duration. It is our impress on that this can be minimized by not forcing the suspension into the sk n too superficially.—Eds.]

Hydrocortisone in Necrobiosis Lipoidica Diabeticorum. R. H Marten and M Dulake[7] (King s College Hosp London) treated 18 lesions of necrobiosis lipoidica diabeticorum in 4 patients with local injections of hydrocortisone Four lesions were treated with a solution containing 50 mg hydrocortisone acetate/ml normal saline containing 0 3% sodium carboxymethyl cellulose and 14 lesions were treated with a solution containing 25 mg/ml As controls 5 lesions were treated with the base solution only The volume of hydrocortisone solution injected depended on the size of the lesions and varied from 0 05 to 2 ml The amount often decreased as improvement occurred Injections were given at weekly intervals varied in number from 1 to 12 and averaged 4-6

Nine lesions treated with hydrocortisone injections disappeared completely or showed only residual discoloration In 8 lesions there was marked improvement but slight elevation or induration persisted. One lesion showed only slight improvement. Injections containing 50 mg/ml were no more effective than those containing 25 mg/ml Three control lesions were unchanged and 2 showed slight improvement Histologic sections taken at various intervals during treatment with hydrocortisone showed all gradations between the fully active lesions and complete healing by fibrosis. Partly healed lesions showed a decrease in the number of chronic inflammatory cells and disappearance of the degenerate areas of collagen

Response to treatment appeared to be independent of the age of the patient, duration severity and control of diabetes and age of the lesions The site of the lesion did not appear to influence response to treatment except that lesions directly overlying bone were often more difficult to inoculate and were prone to ulceration Injection especially in the case of larger lesions were often difficult and painful at first

(7) Brit. J Dermat. 69:395-399 November 1957

but with continued treatment the lesions became softer and the solution spread easily and painlessly

Ulceration in which hydrocortisone injections were considered to have been a precipitating factor occurred on 3 occasions. Two ulcers followed injections of the 50-mg solution and occurred within 24 hours of the first injection in 1 case and after 6 injections in the second case The third ulcer occurred a few hours after the first injection of the 25-mg solution. When the ulcers healed they did so with apparently normal scar tissue. A further complication was the development of cellulitis in 2 patients

► [The fact that ulceration of necrobiosis lipoidica lesions followed local injection with hydrocortisone is noteworthy In our experience to date, when hydrocortisone has been injected into tissues underlying hypertrophic lichen planus (also of the shin) alopecia areata (on the scalp) and chronic discoid lupus erythematosus over the malar region, in no instances have we seen ulceration Apparently lesions of necrobiosis are prone to ulcerate after *injections of hydrocortisone*.—*Eds*]

Hair Regrowth in Alopecia Areata and Maligna Following Intracutaneous Injection of Hydrocortisone. K. W. Kalkoff and E. Macher[4] (Marburg Germany) injected about 50 mg hydrocortisone (in 2 cc.) intracutaneously daily in up to 20 single wheals, into the scalp of patients with alopecia maligna in whom hair growth had been absent for many

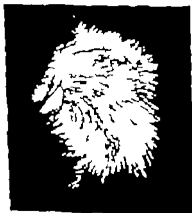


Fig —Spontaneous (white) and provoked (pigmented) hair growth side by side in an areata lesion. Provocation achieved by administration of hydrocortisone several times. (Courtesy of Kalkoff, K W and Macher E Hautarzt 9 443-451, October 1958.)

(4) Hautarzt 441–45 October 1958

years Injections were given at the border of the cutis and subcutis and not too deeply Similar treatment was given to patients with alopecia areata Results were checked clinically and histologically

In the patches of alopecia areata and maligna regular growth of pigmented hair of normal thickness limited to the areas of injection was observed 3-5 weeks after the injections (Fig 1) The lymphocytic infiltrations characteristically found around the papilla and the hair bulb disappeared under the influence of hydrocortisone and pigment formation began again in the matrix. Intracutaneous injections of hydrocortisone did not stimulate any hair growth in alopecia atrophicans or in alopecia prematura

The practical value of the hydrocortisone effect is limited since in the non self limited cases of alopecia areata the patient loses his hair again after the effect has subsided.

► [The dermatologist has the advantage of having available the systemic, topical and intracutaneous routes of administration for hydrocortisone and its analogues each with its own indications for the management of certain diseases of the skin —Eds.]

Vibrapuncture Technic in Treatment of Localized Neurodermatitis Preliminary Study on Effect of Hydrocortisone Acetate Injected by Multiple Vibrapuncture Method into Areas of Lichen Simplex Chronicus is presented by Joseph N Aaron Irwin Kantor and Harold Stromeyer[9] (Mount Sinai Hosp., New York) Five patients with lichen simplex chronicus of long duration were treated The Conway Dermajector was used with needles set for 2 3 mm length. The most effective oscillation rate of the needles was 3 000-3 500 rpm A suspension of hydrocortisone acetate containing 25 mg /cc. was used. All patients tolerated the procedure without anesthesia. All had relief from pruritus within 24 hours and clinical improvement in the appearance of the lesions resulted in each case. The number of times each area was treated depended on the degree of lichenification No residual atrophy was noted during or after treatment All patients who were treated had proved resistant to other forms of therapy

► [Apparently the principal advantage of this mode of administration of hydrocortisone suspension over intracutaneous injection is that it does not produce atrophy The question arises whether the absence of atrophy following treatment of lichen simplex chronicus by this method assures

(9) A.M.A. Arch Dermat 77 576 580 May 1958

the therapist that no trophy will occur fter treatment of other dermatoses by the same technic —Eds]

Cadmium Sulfide Suspension in Seborrhea Capitis. William L. Kirby (Bowman Gray School of Medicine) describes a m thod of treating 84 patients with seborrhea capitis

Method —Patients were asked to wet the hai rub in a 2% sus pension of cadmium sulfide shampoo for 3 minutes, rinse the hair thoroughly massage a second application into the scalp for not less than 5 minutes and again rinse the scalp. Shampooing twice weekly was adv sed in the more severe cases and once weekly in the milder ones.

Of 80 patients adequately followed, 79 reported good to e cellent e ults. Six with seborrhea oleosa responded satis fact rily although 2 had used selenium di ulfide shampoo w thout benefit. The scalp condition of 8 with seborrheic dermatitis was satisfactorily controlled in 4-6 weeks. Of 51 with seborrhea sicca, 50 had good to excellent results. One had shampoos twice weekly for 4 weeks without improvement Fifteen had seborrhea steatoides in some, the cond tion was se ere but response was excellent in all. None required m re than 12 treatments.

Most patients with milder forms of seborrhea were able to decrease the frequency of hampoos after 3 or 4 weeks to every 2 weeks and afte 8-10 weeks to every 3 or 4 weeks. There were no complaints of excessive oiliness or dryness after using cadmi m sulfide shampoo No instances of pri mary rritation or sensitivity reactions were encountered

► [New antiseborrheic agents, some marketed as ethical" drugs and others as proprietaries, have become available with such frequency that it is difficult to remember all their names It is also unusual that one can turn on television set without being exposed to the view of gorgeous blonde ho is waving her Lorelei-like hair back and forth to demonstrate the superb effect of new dandruff remover

While w have had satisfactory results ith the cadmium sulfide shampoo as used by Kirby they do not approach the figure of almost 100% Occasionally it causes oiliness, though nowhere nearly as often sele nium sulfide suspension in several of our cases it has caused excessively dry hair —Eds]

Treatment of Warts with Cantharidin is described by William L. Epstein and Albert M Kligman (Univ of Pennsylvania)

Method —A drop of solution containing 0.7% cantharidin in equal parts of acetone and flexible collodion is rubbed over the wart, the application being confined to the wart itself. Paring or other prior

(1) J Invest. Dermat 29 159 160 September 1957
(2) A M Arch. Dermat 77 508 511, May 1958

treatment is unnecessary After the solution dries a small piece of plastic adhesive tape, slightly larger than the wart, is applied. The preparation is kept in place by covering it with a Band-Aid* or gauze dressing It is recommended that the dressing be kept in place until the patient's return in 7 10 days. It may however be removed after 48 hours or less if there is marked pain or tenderness.

Ordinarily a frank blister forms within 24 hours, but personal responses vary The obviously altered dead or blistered skin is debrided with knife or scissors on the next visit. One application is often enough, but reapplication should be made at weekly intervals as long as warty tissue persists.

The authors treated 113 warts in 61 patients Immediate clinical cure lasting at least 3-6 weeks occurred in 66 of 69 ordinary warts 20 of 27 plantar warts 11 of 12 peri and subungual warts and 2 of 5 mosaic warts Many patients required only 1 treatment and most responded to fewer than 3 applications Severe painful reactions occurred in 4 patients Recurrences were noted in 6 of 42 plain warts and 4 of 14 plantar warts followed for 6 months

Cantharidin is no more effective than other destructive technics, perhaps less so than electrosurgery Its virtue lies in its simplicity and lack of residual scarring It is especially useful in the treatment of warts in children

► [Another worthwhile addition to the therapeutic armamentarium for these exceedingly common lesions —Eds]

Local Therapy of Oral Leukoplakia with Vitamin A. Dattatreya N Mulay and Frederick Urbach[3] (Roswell Park Mem'l Inst Buffalo) treated 10 patients with typical oral leukoplakia of 3 months to 10 years duration with oral troches containing 150 000 units of vitamin A each Seventy of the leukoplakia ranged from grades II to IV (Thoma) The patients were instructed to remove their dentures and allow 1 troche to dissolve slowly in the mouth 2 3 times daily Treatment periods varied from 2 to 6 months Seven of the patients showed pronounced improvement with 70% clearing or better 1 slight improvement 2 (1 of whom took the troches only intermittently) no improvement

It is known that a number of medicinally active compounds (cortisone desoxycorticosterone etc) are absorbed easily through the mucosa even though they penetrate the intact skin poorly The present results indicate that vitamin A penetrates plaques of oral leukoplakia when applied topically

(3) A.M.A. Arch Dermat 78 637-638, November 19 8

The beneficial effect probably is connected with interference with pathologic keratinization. Duration of the beneficial effect was not determined.

► [It is difficult to assess the efficacy of topical treatment in oral leukoplakia unless the condition is very pronounced and disappears completely under treatment and unless similar troches not containing vitamin A ha been used in control cases.—Eds.]

Chloranil in Treatment of Psoriasis Substitute for Chrysarobin. Walter O Teichmann and Peter N Horvath (Washington, D C.) treated 93 patients with psoriasis with 5 or 10% chloranil (tetrachloro p-benzoquinone) in a poly ethylene glycol base. Patients were nstructed to apply the ointment thinly at bedtime and to rub it in thoroughly so no excess remained. Chloranil stains the skin a light brown, which usually is not troublesome if desired it may be removed with a fat solvent such as petroleum benzin.

Considerabl improvement was observed in 55 patients moderate improvement in 24 and no improvement in 10 The p ocess of resolution is similar to that of chrysarobin or coal tar therapy The lesions first lose their scales, become less elevated and n the most esponsive cases finally break up into small areas and fade away The most marked improvement was observed during the first month of treatment. In several patients, the lesions retrogressed when treatment was topped and mproved again on reapplication of the drug No posttreatment leukoderma was noted. Chloranil was most ffecti e against the typical psoriatic plaque characterized by heavy scales. It appeared to benefit palma and plantar plaques nd intertriginous lesions but was least effective against small guttate lesions. Control areas treated with ointment base showed no improvement in 10 of 24 patients slight improvement (not equivalent to that of areas treated with hloranil) in 12 and improvement equal to that of areas t eated w th chloran l in 2 patients.

One instance of true sensitization to chloranil was observed. In 3 other patients primary irritation resulted from use of 10% ointment, but not with 5%

► [W have tried this compound in eaker concentration and only in seborrheic dermatitis and psoriasis of the scalp In some of the cases it seemed to be quite effective —Eds]

New Approach to Control of Acne Vulgaris. Because at

) South M J 46 1331 1333, December 953

times acne vulgaris is more severe in tropical climates where sweating is increased Thelma Golub Warshaw[5] (New York Infirm) assayed the clinical effect of decreased sweating on patients with this disease After each face wash 33 patients applied 20% aqueous solution of aluminum hydroxychloride to the entire face except the periorbital area Treatment was continued for 3 weeks to 6 months All patients also used topical preparations containing resorcin and sulfur and were given routine instructions on the care of acne vulgaris. A control group of 33 patients received similar treatment except that aluminum hydroxychloride was not used.

Clinical improvement with a decrease of comedones oiliness and pustules was observed in 32 of the 33 patients treated with aluminum hydroxychloride The aluminum preparation seemed to accelerate initial clearing and easily maintained the skin in a less oily acne-free condition The only side effect reported was the deposit of a saltlike substance on the skin that could be removed easily by washing Improvement was less rapid and less well maintained in the control group.

The rate of fat (sebum) spreading over a wet skin is of the order of at least 10^3 times the rate of flow and spread on a dry skin Also variations in the level of ether-soluble substances (fats) on skin directly parallel the level of sweat delivery in the skin area. Thus the use of an aluminum salt as an antiperspirant and consequently as an empiric sebaceous gland inhibitor seems logical

► (In our experience aluminum hydroxychloride solution or similar preparations sometimes aid in decreasing the oiliness of the face in patients with or without acne vulgaris.—Ed)

Primary Irritant Activity of Barrier Creams J Tas[6] (Hadassah Univ Hosp Jerusalem) performed 48-hour patch tests with 6 different barrier creams on 300 patients most of whom had eczema Oil resistant creams caused a high percentage of positive reactions Kerodex* B D gave 49.7% and Magnor red 25% positive reactions The water resistant creams, Magnor white (14.7% positive) and Kerodex B W (3.7%) showed a much lower incidence of positive reactions The percentage of positive reactions with silicone creams was still lower positive reactions with Covicone* occurred in 2% and with Silicote in 0.7% of cases

(5) New York J Med 7 [illegible]-4000, Dec 1 1 7
(6) J Invest Dermat 29 [illegible] 125, September [illegible]

Most reactions were of the primary irritant type characterized by circumscribed erythema or by a blister but in 5 instances eczematous reactions were observed. The high incidence of positive reactions to some of the creams does not detract from their considerable prophylactic usefulness. Actual use of the barrier creams in which they are applied for a few hours without covering is different from application for 48 hours under an occlusive bandage as in patch tests. The well-known clinical fact that barrier creams easily provoke exacerbation in inflamed skin can be explained by the slightly irritant action of the creams. Therefore, they should be used only on healthy skin for prophylactic purposes.

► [The high degree of primary irritancy of some of these creams itself presumably severely limits their use. There is very little discussion now of barrier creams as compared with a few years ago. We suspect that this is due to the generally poor results with these "protective" creams.—Eds.]

Experimental and Clinical Studies on Mode of Action of Atabrine and Chloroquine in Chronic Lupus Erythematosus were conducted by A. Wiskemann and H. Koch (Univ. Skin Clinic, Hamburg Eppendorf, Germany). When compared with commonly used, commercially available light-protective ointments, 10% atabrine and chloroquine emulsions, 10% showed effective light protection from erythema-producing ultraviolet light of medium wave length. About 30% of the light-protective action is probably not absorptive but biologically determined. When the ointments were applied immediately after exposure to ultraviolet light, no biologic light-protective effect could be demonstrated.

Butazolidin administered intramuscularly increased the ultraviolet erythema threshold only when it was given before the radiation.

The "biologic light-protective effect probably consists of a nonspecific antiphlogistic action. After 3 days of administration atabrine and chloroquine showed a definite antiphlogistic effect in the rat paw test. The dose used corresponded to 5 times the maximum daily human dose. The antiphlogistic effect was less pronounced than that of cortisone. The superiority of atabrine and chloroquine over cortisone in the treatment of chronic lupus erythematosus is probably due to different modes of action and different distribution in various organs.

[7] Hautarzt 3:15 18, May 1952

In 22 patients with chronic lupus erythematosus who did not receive any chloroquine by mouth for at least 4 weeks 8 weeks of therapy with chloroquine ointments was ineffective. Since the light protective effect of the ointments must be superior to the protection offered by oral administration of the same drugs it can be assumed that the absorptive light protective effect of chloroquine does not play an important role in the treatment of this condition The antiphlogistic action of the ointments was not effective either

In experimentally photosensitized or pathologically photosensitive skins chloroquine ointment also gave protection against ultraviolet light of long waves. This was considerable when the maximum absorption capacity of chloroquine at 320-340 mμ and the wavelength of the causative light corresponded with each other

So-called Decubitus Ulcer Pathogenesis, Prophylaxis and Treatment are discussed by L Justin Besançon H Pequignot, J P Etienne J Savier and R. Vilain [8] Pressure on points of contact aggravated by loss of sensitivity and mobility and by impairment of muscular tone gradually or suddenly produces a true infarct of the soft tissues which leads to ulceration The course of the ulcer evolves in three stages elimination of necrotic material filling and marginal epidermization

Prophylaxis of this complication demands a judiciou evaluation of the risk by the physician correct interpretation by the nurse of the lesion at onset when still reversible and use of preventive methods especially ma sage On admis ion patients should be divided into major and minor risks The former are placed immediately on the alternating mattres and are given massage twice daily In pection of buttocks and heels requires turning once or twice daily and placing a groove for the heels Major risk patient include all thos who are completely immobile with lo s of en itivity i e tho e with comas of all types hemiplegia paraplegia, cachexia with decreased movement and serious heart failure In min r ri k patients, a single daily massage is sufficient but pres ure points should be inspected each day and if the cutane u c n dition is not being controlled pr phylaxi i stepped up with 2 massages a day on the special mattre

(8) Semaine hôp Paris 33 4115-4121 Dec 1 1 7

Once decubitus has developed, general treatment should consist of control of anemia and malnutrition by small transfusions of blood and deplasmatized erythrocytes. Tube feeding often is inadequate and every effort should be made to re-establish normal feeding by mouth. Local treatment has two objectives: to correct the atrophy and to cleanse the lesion. Massage should not be discontinued because it favors vascularization of the defect, accelerates elimination of devitalized tissues and prevents trochanteric or ischiatic lesions. If the patient cannot move spontaneously in lateral decubitus, the alternating mattress permits still vital tissues on the periphery of the ulcer to maintain trophicity. On the denuded plaque a daily lavage with soap or detergent, combined with a rub with alcohol is an excellent prelude to massage. A dressing is unnecessary. For dry ulceration a dressing is also useless; excision is the only effective measure but this is usually impossible since the underlying disease is at its height. When general state improves and the ulcer commences to become detached, the black plaque may be excised and the resection should be sufficiently extensive to remove all necrotic tissue. A dry dressing should be applied. A sheet of cellophane separates the body dressing and protects the cloth from oozing. A body bandage is preferable to adhesive which often causes erythema. To aid in surgical drainage, Dakin's solution and trypsin powder are used.

When the wound is completely freshened, cicatrization is inevitable but it is sometimes retarded by permanent dorsal decubitus position (paraplegics), malnutrition, encroachment of skin at the edges of the lesion which may delay the regeneration of marginal epidermis, and an ulcerated callus which resists spontaneous scarring.

► [The American version of the alternating mattress is made of plastic and consists of a series of tubular longitudinal spaces which alternately are filled with air and then collapsed. This is done by means of an automatic pump. To produce a massaging action every other tube is filled while the in-between ones are left collapsed. At appropriate time intervals the collapsed tubes are filled and the filled ones are allowed to collapse, thus producing a continuous and regular massaging action.

Proteolytic enzymes other than trypsin are available in this country and are used to debride necrotic ulcers.—Eds.]

Preventive Measures against Skin Injuries from Cold Wave Developers are outlined by Siegfried Borelli[9] (Univ

(9) [illegible] 1 540-544, December 1957

of Munich) Compounds used in making cold waves (permanent) affect the skin in two ways they cause swelling and loosening of the corneal layer and exert a nonspecific alkali effect Hyperhidrosis may also develop The simultaneous use of thioglycol and alkali increases these effects and preventive measures must be directed against them To prevent both but especially the keratolytic effect, hairdressers have been advised to treat with H_2O_2 and an acid rinsing solution after each application not only the customer's hair but their own hands. The aim is to neutralize the effect of thioglycol Unfortunately most hairdressers have not followed these suggestions and even refused them with the excuse that the *fixing solutions irritated their skin*

More than 200 hairdressers engaged routinely in preparing cold waves were studied concerning the best method to *protect the skin of their hands Use of the usual fixation solutions* alone did not give any protection and often even aggravated the skin changes Application of fatty ointments seemed to be the most effective Various ointments gave practically the same benefit as long as they contained some fat. The best protection was achieved when the hairdresser applied some fatty ointment to his hands before each cold wave application and rinsed his hands with the fixing solutions afterward followed again by a fatty ointment The simultaneous application 2 or 3 times daily of an astringent such as Taktokut (symm dichlorphenylsulfonyl polyamino benzolsulfonyl-di-aminophenylsulfonacetic ammonium) which is a synthetic tanning agent, will effectively suppress hyperhidrosis.

B Systemic Drug Therapy

Experimental Ringworm in Guinea Pigs Oral Treatment with Griseofulvin is described by J C Gentles[1] (Univ of Glasgow) Griseofulvin a metabolic product of several penicillium species is markedly fungistatic to many fungi in vitro and in plants it shows systemic antifungal activity It is reported to have low mammalian toxicity

Guinea pigs were infected with Microsporum canis and treatment with griseofulvin was started 10 days later when

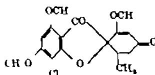
(1) Nature, London 182:476-477 Aug 16, 1958

lesions were well developed. Daily dosage was 60 mg /kg control animals were given unmedicated tablets Clinical im provement was noted within 4 days, and the highly inflam matory reaction which occurred in all control animals was prevented in the treated guinea pigs. Among the latter group about half the hair follicles were shown histologically to be infected after 4 treatments By the 8th treatment few infected follicles could be found. Skin sections of the untreated ani mals showed heavy infection of almost all hair follicles at this time. Under Wood light, nfected hairs of treated animals fluoresced only at the tips, nd microscopic examination re vealed the dermatophyte only in the upper part of the hair shaft. Apparently the uninfected part of the hair formed during treatment, was resistant to invasion by the fungus.

Similar experiments have indicated that griseoful in s equally effective when given orally to guinea pigs infected with Trichophyton mentagrophytes. It has also been used successfully in treatment of T verrucosum ringworm induced in cattle. In vitro it s active in low concentrations against all the common dermatophytes.

► [This report, while dealing with the effects of griseofulvin in fungous infected laboratory animals, is likely to turn out to be one of historic im portance in dermatology If these results in laboratory animals and the preliminary favorable results thus far obtained in man are not marred by as yet undiscovered prohibitive side effects, w may be on the threshold of the era of truly specific systemic control of superficial fungous infections

The chemical structur of griseofulvin has been reported to be



Apparently the drug has fungistatic rather than fungicidal properties and its unique therapeutic efficacy is based on its selectiv capacity to combine with keratin Since its chemical constitution is known, ther is no reason hy the chemists should not be able to provide us with related compounds ith different and perhaps better therapeutic efficacy

Among the innumerable questions which will have to be answered are Can fungous infections truly be eradicated by single course of griseoful vin or will repeated courses of treatment be necessary as is often the case in the management of furunculosis with broad-spectrum antibiotics? If single courses are effective, how long will the drug have to be given? Will some strains of fungi develop resistance?

Apart from its promise as pecific therapeutic agent for some of the most common dermatoses, griseofulvin may turn out to be wonderful

tool for the scientific investigation of the mechanism underlying resistance and susceptibility to superficial fungous infections. Further it may help in solving some of the more puzzling clinical syndromes connected with fungous diseases, such as, which eruptions are or are not "ids" Perhaps some dermatologic entities hitherto suspected or unsuspected of having a fungous etiology will be shown definitely to be caused by a fungous infection.

Dr Harvey Blank, of the University of Miami reported at the December 1958 meeting of the American Academy of Dermatology and Syphilology on the therapeutic effectiveness of griseofulvin administered systemically in the management of certain superficial fungous infections of the skin. Although the number of patients treated was limited and the follow up period short, this antibiotic promises to be a distinct contribution to dermatologic therapy —Eds]

Disseminated Coccidioidomycosis Treated with Amphotericin B Amphotericin B is an antibiotic derived from a species of streptomyces found in a soil sample from Venezuela [illegible] a wide variety of [illegible] In vivo it has an [illegible] infected with C immitis

Robert C Hunter Jr and Edward S Mongan[2] (William Beaumont Army Hosp) treated 4 patients with disseminated coccidioidomycosis with amphotericin B One received about 5 Gm daily by mouth for 38 days He was already recovering when the drug was started and there was no reason to believe it altered the course of the disease Three were given amphotericin B intravenously for 3-12 months and all 3 reacted predictably with anorexia nausea chills and fever after every infusion Severity of the reactions tended to decrease slightly with continued medication Salicylates and antihistamines did not alter the reactions All 3 patients had elevated blood urea nitrogen one or more time during treatment which subsided on interrupting treatment for 1 2 weeks. Because of the side reactions the dose was limited to 50 mg in 5% dextrose solution which wa given [illegible] over 6 hours every other day after supper

Results of treatment in a disease a unpredictable a di seminated coccidioidomycosis mu t be accepted with caution All 3 patients improved while on intravenou amphotericin B therapy but response was slow After months of treatment C immitis could be cultured from a ariety f area in the e patients. In 2 of the patients, 20-25 mg amphotericin B a injected directly into 7 coccidioidal ab cesses 1 3 times about

(2) U S Armed Forces M. J 9 1474 1486, October 1958

1 week apart. Response was uniformly favorable and fluctuation disappeared in 3-6 weeks.

Results with amphotericin B intravenously indicate that it possibly was useful in treating disseminated coccidioidomycosis. Results with direct injection of abscesses were more impressive. Amphotericin B probably represents the first real ad ance in treatment of dissem nated coccidioidomycosis but further cl mcal testing is essential.

► [With griseofulvin, amphotericin B and Mycostatin® it certainly looks as if the specific systemic or local antibiotic treatment of superficial and deep mycoses soon will be as much of routine as the sy temic and local treatment of most bacterial diseases. Unfortunately no similar progress has been made in the specific antibiotic treatment of irus diseases. Successful intralesional injection therapy with amphotericin B in chromoblastomycosis of the skin and subcutaneous tissues has been reported by Costello, DeFeo and Harber.—Eds.]

Effect of Oral Steroid on Noninflammatory Scalp Ringworm: Preliminary Report. In a case of scalp ringworm in a boy aged 8, Naomi M. Kanof[3] (Children's Hosp., Wa h ington, D. C.) bserved complete clear g in 6 weeks with oral systemic steroid therapy (5 mg. prednisone 4 times daily). In 8 subsequent patients with noninflammatory tinea cap tis due to Microsporum cani no complete cure has yet been chieved. After 4-10 weeks' therapy howe er all pa tients demonstrated markedly fewer broken-off fluorescent hairs or a change of the fluorescence from brilliant emerald green to grayish white. All patients had been refractory to t pical therapy and had in olvement of at least two thirds of the scalp before stero d therapy was initiated.

Further obser tions will be necessary to determine wh ther improvement will continue nd permanent cure can be a h eved. It is not known whether the marked decrease in the numbe f flu escent hairs and the hange in the hue of fluorescence are d nc of an alt ration in the infection proper or only change in th phenomenon of fluorescence or wh the th hair growth has been altered n such a manner as t retard r eject fu gu nvasion.

► [Irrespective of hether oral steroids will eventually prove to be therapeutically effectiv and desirable in scalp ringworm, these findings are of the greatest theoretical interest. What is the mechanism which brings about these striking changes? I it, as Naomi Kanof suspects, an effect on the hair cycle? Is it an effect on the fungi via direct or indirect pharmacologic action of the steroid compound or is it some other ffect? —Eds.]

(3) J. Invest. Dermat. 3: 39, September, 58.

Effects of Triamcinolone (Aristocort®) and 6-Methyl prednisolone (Medrol) on Some Skin Diseases Therapeutic Note is presented by F Kalz[4] (Montreal) Triamcinolone was used in the treatment of 48 patients including 24 with severe atopic dermatitis 16 with other eczematous eruptions 6 with psoriasis 1 with pemphigus and 1 with alopecia areata. Treatment was started with 20 mg daily for 2 5 days, and the dose was then reduced by 4 mg every 2 3 days until the minimal effective dose was found. Response was satisfactory in all patients except 4 of the 6 with psoriasis In 21 of the 24 patients with atopic dermatitis a satisfactory maintenance dose averaging 6 mg daily could be established. Three of these patients had side effects

Untoward side effects occurred in 8 patients in the entire group Epigastric pain occurred in 4 1 of whom showed reactivation of a duodenal ulcer Four patients had headaches and dizziness Minor side effects consisted of hyperhidrosis in 2 patients and acne in 1

Six patients who showed side effects with triamcinolone were given 6-methylprednisolone and all tolerated the drug well A number of other patients were treated with 6-methyl prednisolone alone At least one third higher dosage was required to obtain the same effect as with triamcinolone In 2 patients 6-methylprednisolone caused dizziness and tiredness These patient were able to take dexamethasone without side effects

Triamcinolone offers several advantages over prednisolone. It does not cause sodium retention it rapidly controls the inflammatory phase of skin diseases and the effective maintenance dose is low Its disadvantage is a high incidence of minor side effects Though 6-methylpredniso l ne is less potent it is less apt to cause side effects

► [Both triamcinolone and methylprednisolone a e luable ddition to the corticosteroid armamentarium among their princ pal ad antages is *the absence* of sodium- and water retaining pr perties Apparently corti sone and ll its analogues so far used therapeuticall ha the capacity to produce weakness and muscular dystrophy p ovided the dose large enough and the period of administration prolonged However w th triamcinolone this side effect is encountered more often When muscle weakness develops with the use of any of the corticosteroids, r ACTH they me have to be withdrawn before recovery of muscle trength observed

Dexamethasone although effective in much maller d ses than the other

(4) Canad. M A. J 79 400 401 Sept 1 19 5

corticosteroids, produces side effects at these lower dosages similar to the other produced at the high dosage level —Eds]

Use of Triamcinolone (Aristocort®) in Selected Dermatoses. Results in 13 patients are described by Ben Kanee[3] (Vancouver) Of 2 patients with systemic lupus erythematosus, 1 did well initially with prednisone but required 30 mg daily for maintenance. This dose resulted in moonface and some acne. On changing to triamcinolone, there was no improvement in the facies on a required daily dose of 24 mg Hirsutism, dilated venules telangiectasia on the lower extremities and tiredness occurred on this dose On changing to methylprednisolone the daily requirement was reduced to 18 mg, and the patient felt better subjectively although features similar to Cushing's syndrome were retained The second patient, originally maintained on cortisone, showed considerable improvement with prednisone and now is showing still greater improvement with a maintenance dose of 14 mg triamcinolone

A patient with generalized scleroderma has been on a maintenance dose of 8 mg triamcinolone for 7 months, as compared with 15 mg prednisone previously She has shown comparable clinical and subjective improvement, though she is gradually losing weight, and has bouts of anorexia and diarrhea, which may be due to the drug or to intermittent influenza

Two patients with dermatitis herpetiformis failed to respond to triamcinolone in doses of 16-32 mg daily Triamcinolone, 16 mg daily appeared to exert a favorable influence in the experimental treatment of 2 patients with alopecia areata Six patients with extensive and pruritic psoriasis showed a marked clinical and subjective response while being maintained on doses of 8-12 mg daily

Triamcinolone was stopped in only 1 instance because of side effects (symptoms of gastric ulcer with negative radiograph) Otherwise side effects were minor including features of Cushing's syndrome—moonface hirsutism acne, telangiectasia, dizziness, flushing lack of energy tiredness and loss of appetite.

► [From the dermatologic viewpoint perhaps the most important feature of triamcinolone is that it unquestionably appears to be in general more efficacious in psoriasis than the older and other newer steroids —Eds]

[3] Canad M A J 79 731, Nov 1, 1958

Triamcinolone in Treatment of Systemic Lupus Erythematosus. Edmund L Dubois[6] (Univ of Southern California) treated 29 patients for up to 11 months Triamcinolone, an unsaturated prednisolone derivative, is 1 3 times as powerful as prednisone and 4 4 times as potent as hydrocortisone as an anti inflammatory agent. The amount of triamcinolone required by individual patients varied widely depending on the severity of the disease and sensitivity of the patient to the agent. The average initial dose in a patient with a mild case of systemic lupus erythematosus was 20 6 mg daily The average maintenance dose used to control mild exacerbations was 26 mg daily There was no evidence of sodium retention or potassium loss Routine sodium restriction potassium supplementation and prophylactic ulcer diet were not used

Repeated gastrointestinal x ray studies in 16 patients revealed evidence of peptic ulceration in only 1 who received 96 mg daily No changes were observed in 9 who had gastric analyses with histamine every 2 months or in 13 who had 24-hour uropepsin determinations.

The pattern of clinical improvement closely paralleled that obtained by previous treatment with older steroids All clinical and laboratory abnormalities except long standing renal involvement disappeared A major difference between *triamcinolone and other steroids was a tendency in 18* patients toward progressive gradual weight loss averaging 7 8% of initial body weight.

Cutaneous side effects particularly cushingoid appearance hirsutism and striae were more marked in women taking triamcinolone than with older steroids. The most serious side effect was muscle weakness which appeared in 6 patients after 4-32 weeks of therapy There seemed to be no relation between dosage and this symptom The profound muscle weakness most marked in the quadriceps groups gradually cleared after several weeks of therapy with another steroid. Male patients did not show these side effects. Of 14 patients who had received prior steroid therapy with all the older anti inflammatory hormones 7 felt better and their disease was better controlled with triamcinolone

Treatment of Psoriasis and Other Dermatoses with Triamcinolone (Aristocort[*]) *Walter B Shelley Joseph S*

(6) J.A.M.A. 167:1590-1599 July 26, 1958.

Harum and Donald M Pillsbury[6] (Univ of Pennsylvania) treated 60 patients who had all forms, types and degrees of psoriasis with triamcinolone, a corticosteroid, in doses of 12 16 mg daily by mouth. In 36, response was prompt and unquestionable within a week the scaling and erythema diminished significantly and within 2-4 weeks of continued adequate dosage the psoriasis in some was completely erased. This group presented the distinctive finding of local involution of psoriasis at the site of injection of triamcinolone intradermally Relapses invariably occurred when the drug was withheld. In view of the rapid relapse that invariably followed suspension of therapy reduction of the dose to zero will probably offer great difficulty in many patients. Topical use was without effect.

A wide variety of reversible side effects was observed. Some were favorable such as stimulation of hair growth in alopecia areata, but many were unfavorable, such as flushing hyperhidrosis facial hirsutism and facial contour changes. Triamcinolone proved remarkably effective in treatment of alopecia areata This compound seems to have a specific stimulant effect on hair growth.

Triamcinolone was highly antiallergic, antirheumatic and anti-inflammatory and therefore useful in various dermatitides Its use in psoriasis should probably be limited to acute extending cases that are not controllable by other means or to extensive severe chronic forms. In common with all other antipsoriasis remedies this drug is no cure for psoriasis. It must be recognized as purely palliative. Triamcinolone is a strong corticosteroid with influences throughout the entire body It is not to be given for relief from a few scales on the elbows

Combination of Chloroquine and Prednisone in Treatment of Lupus Erythematosus was tried by A Midana and M Depaoli (Turin Italy) in 18 patients having chronic and subacute cases with localized and disseminated lesions. The daily dose of chloroquine was 500-600 mg for 8-10 days, then 250 mg for 4-8 weeks 15 mg prednisone was given daily for 10 days and 10 mg daily for 4-8 weeks.

Comparison of results with those obtained with chloro-

(6) J.A.M.A. 167:[illegible], June 21, 1958
(7) Dermatologica 115:[illegible], November, 1957

quine alone showed that with the combined treatment there was more rapid fading of the lesions and absorption of the edematous infiltrative process, which in some cases was striking These results were observed not only in circumscribed local lesions but also in 2 of 3 patients with disseminated distribution in the extremities. With addition of prednisone, chloroquine was better tolerated and complete courses of the drug could be given without troublesome side effects. These results support the conclusions of others who have used cortical hormones combined with prolonged antibiotic and chemotherapeutic administration with good effect.

Two possible explanations of the potentiating effect of small doses of cortical hormone are suggested (1) The profound effect of prednisone on the function metabolism and proliferation of cells may lead to an increased concentration of chloroquine in the plasma, owing to its retarded elimination (2) Slowing of the progressive encapsulation of foci by the hormone may lead to a greater concentration of chloroquine in these areas, with more rapid regression of clinical manifestations

► [In subacute or acute disseminated lupus erythematosus as in other diseases, it makes good sense to use in combination two therapeutic agents each of which by itself is capable of benefiting the disease With two such effective systemic medications given simultaneously it is usually possible to reduce the required dose of both drugs, thus lessening the chances for possible undesirable effects produced by each alone At times of course greater beneficial effects can be achieved with such combined treatment than with either drug alone.—Eds]

Scleroma Neonatorum Report of Three Cases Treated with Cortisone is presented by P C Bajpai P Singh and U Bhatia[8] (Lucknow Med College)

CASE 1—Boy aged 15 days had dyspnea feeble pulse diarrhea and rapid, shallow respiration The skin over the body except for the palms, soles and scrotum was thickened and indurated without pitting Treatment included oxygen, subcutaneous and oral electrolyte solution, Chlorostrep® for diarrhea and cortisone 5 mg daily for 2 days, then 10 mg daily for 5 days Improvement was evident in the skin and general condition after 48 hours By the 8th day the skin was entirely normal Recovery was complete in 10 days

CASE 2—*Boy aged 10 days was critically ill with feeble rapid* pulse rapid, shallow respiration diarrhea abnormal temperature and generalized waxy pale thickened skin. Cortisone was administered in doses of 5 mg 3 times a day for 3 days, 10 mg twice a day for 4 days and was then tapered off *Improvement in the skin was* no-

(8) Indian J Pediat. 24 207 212, July 1957

ticeable on the 3d day and the child seemed well except for diarrhea by the 6th day. Symptoms of septicemia developed on the 10th day however and the child died the next day.

CASE 3.—Boy aged 3 months, had had diarrhea for 12 days. The skin on the legs, forearms and lower abdomen was stiffened and slightly thickened. Dehydration and subnormal temperature were present. Induration of the skin became more extensive, despite treatment with fluids and sulfaguanidine but began to subside 3 days after cortisone and penicillin were started. The child was well 6 days later.

The authors feel that cortisone was primarily responsible for the improvement observed in these 3 patients. During the past year 10 infants were treated without cortisone in Children's Hospital and Queen Mary's Hospital in Lucknow. In each, the sclerema neonatorium was fatal.

► [Another report attesting to the often lifesaving and therefore curative effect of corticosteroids in this disease.—Eds.]

Pemphigus Vulgaris under Prolonged Massive Treatment with ACTH and Cortisone. I. Urinary 17 Ketosteroid and 17 Hydroxycorticoid Excretion. As some authors have described low values of 17-ketosteroid excretion as characteristic of pemphigus, A. Dostrovsky and F. G. Sulman[9] (Jerusalem) studied this problem before starting treatment in 21 cases of pemphigus. Though within normal range, the titer of 17 ketosteroid excretion in the urine of these patients tended toward low values, and there was an unusual fluctuation of 8-28 mg./day not found in normal persons or in those with other diseases. There was no noteworthy difference in 17 ketosteroid values during the period before treatment due to sex, duration of disease or severity of attack. There was no parallel between the titer of urinary 17 ketosteroid excretion and the result of the Thorn test.

In 12 patients with generalized pemphigus vulgaris, the 17 ketosteroid excretion was further studied under massive treatment with cortisone and ACTH during exacerbation and quiescence. Treatment routines used were ACTH alone, cortisone alone, alternating with ACTH and combined ACTH and cortisone.

ACTH stimulated 17 ketosteroid excretion in all cases of active pemphigus, particularly in the first attack and also in most relapses. One case was refractory. Cortisone inhibited 17 ketosteroid excretion. The effect, though not constant, was evident even with small doses both in active stages and

(9) Dermatologica 1 43 96, February 1958

during remissions occurring on a maintenance schedule of 100-150 mg daily Depression was less marked in males than in females because the gonadal part of the 17 ketosteroid excretion in the male is not subject to depression by cortisone Depression did not occur when cortisone was alternated with ACTH Combined ACTH and cortisone therapy initially had no inhibiting effect on 17 ketosteroid excretion because of the corticotropic action of ACTH In later stage extreme oscillations occurred apparently due to an antagonism between the stimulating effect of ACTH and the inhibiting effect of cortisone.

The pattern of 17 ketosteroid excretion depended only on the hormone treatment and not on the severity of the disease. However 17 ketosteroid titers were lower in cases of relapse than in first attacks This was apparently due to exhaustion of the adrenal gland caused either by the disease or treatment. Spontaneous recovery of an exhausted adrenal gland was evidenced by a sudden increase in 17 ketosteroid excretion but a decrease to zero sometimes occurred despite energetic ACTH treatment, indicating complete exhaustion of both adrenal glands

A paradoxical pattern of 17 ketosteroid excretion was encountered in some patients who received massive doses of cortisone (up to 900 mg daily) resulting in extremely high 17 ketosteroid excretion This also occurred sometimes in patients receiving cortisone alone after being previously stimulated by ACTH This paradoxical reaction could be explained as due to a change in the metabolic processes in the adrenal gland and the liver by which a high ratio of the cortisone administered was converted into 17 ketosteroid as long as the adrenal gland was completely suppressed.

The pattern of 17 hydroxysteroid excretion examined in 9 patients was fairly uniform Normal values were 2 12 mg daily When treatment with cortisone and/or ACTH was started these values went up immediately eventually representing an excretion of up to 40% of the cortisone administered It seems therefore, that up t thi amount the drug may be excreted as tetrahydrocortisone in the urine

It is evident that neither 17 keto teroid nor 17 hydroxy corticoid excretion provides a reliable diagnostic or prognostic aid in pemphigus vulgaris Therapeutically l w 17

ketost roid values are a useful guide, since they indicate when and at what dosage addition of ACTH to the routine cortisone treatment becomes necessary

The data allow interesting insight into the complicated mechanism of the ACTH-cortisone relation and its manifestations in pemphigus, especially in the later stages when exhaustion of the adrenal glands becomes unavoidable The authors experience shows that the result of such exhaustion is never complete atrophy of the adrenal gland, but a periodic unresponsi eness which eventually results in spontaneous recovery A rapid method of determini g 17 ketosteroid ex cr tion in these cases would allow early diagnosis of impending exhaustion and permit well timed prevention by addition of appropriate doses of ACTH to the cortisone schedule

► [There are tw schools of thought about the desirability of giving ACTH simultaneously with cortisone or its analogues According to one school, it is useless to administer ACTH while the patient is receiving oral cortisone because of the suppression of adrenal cortical activity produced by the ortisone Also, current concepts suggest that pituitary gland function is depressed by the administration of ACTH and this in turn further reduces adrenal cortical function The other school feels it is worth while to administer ACTH regularly as it prevents the adrenal cortex from becoming completely suppressed, even though cortisone is being given by mouth The findings of Dostrovsky and Sulman support the latter viewpoint and provide guide as to hen it is desirable to add ACTH injections while cortisone is being given orally —Eds]

Appraisal of New Antipruritic Trimeprazine (Temaril) Law ence C Goldberg and Adrian Diamond[1] (Cincinnati) treated 160 patients with pruritus associated with dermati ti and sy temi disorders. Dosage of trimeprazine ranged from 2 5 mg twice a day to 5 mg every 3 hours. Some patients w th hronic diseases took the drug continuously for 6 weeks. In o er 70% of the patients relief from pruritus a ged from good to excellent. The most outstand ng results were in 32 patients with chickenpox, none of whom had se ere pruritus while taking the drug The drug d d not affect a f the dermatoses except to make them more amenable to outine therapy through decrease of itchi g This was particula ly true of patients with atopic dermatitis.

The commonest side effect was drowsiness noted in 60% of the patients which was controlled by adjusting the dosage One patient had giant urticarial lesions 24 hours after taking the drug and the same effect was noted when the drug

( ) Antibiotic Med & Clin Therap 5 583 584, September 1958

was tried again Agitation was noted by 3 patients and a bad taste after taking the tablets by 1

New Oral Antipruritic. Paul L. Williams[2] (Seattle) treated 90 patients who had severe pruritus complicating acute and chronic dermatoses and systemic diseases with trimeprazine (Temaril) a phenothiazine derivative The usual starting dose was 2.5 mg 3 or 4 times daily Once the severe itching was controlled the total daily maintenance dose if needed was reduced to 5 mg When nighttime itching was severe a dose larger than the usual daytime dose was taken before retiring Treatment lasted a few days to several weeks in acute cases and several months in some chronic cases.

Satisfactory results (complete relief from pruritus) were achieved in 75 5% of cases. Of 22 patient who had unsatisfactory results 14 obtained complete relief from itching but also had side effects and 8 had incomplete relief from itching The antipruritic effect of trimeprazine generally began 1 3 hours after the first dose was taken Of 81 patients with *severe nocturnal itching 83% could sleep without interruption* while taking the drug Of 75 patients who had skin lesions at the time treatment with trimeprazine wa started, 44 had complete healing and 20 had almost omplete healing when the drug was discontinued In 4 patients some evidence of healing wa evident and in 7 no effect n the kin lesions could be detected though pruritus had stopped

Side effect due to trimeprazine included drowsines in 11 patients and lethargy nightmares and a nonspecific skin eruption in 1 each None were serious There was no evidence of tolerance in any patient and therapeutic paradox was not observed Occasionally moderate hypoten ive reactions were seen in patient receiving 20 mg or more trimeprazine daily and antihyperten i e drug Such large doses were rarely required however

► [Trimeprazine is well worth trying in the management of pruritus bearing in mind that the soporific effect i quite marked for some patients In our own experience beneficial results were chieved some hat less often than reported by Williams or Goldberg and Diamond In view of it chemical structure there i a possibility that it may cause photosensit zation similar to chlorpromazine and Phenergan but thus far w ha e not seen or heard of any proved cases A possible exception i boy aged 3 who repeatedly developed blinking of the ey lid pparently due t photophobia, when he wa taking trimeprazine The bl nking disappea ed each time the drug was stopped.—Eds]

(2) Northwest Med. 57 1143 1144, September 1958

Oral Treatment of Keloids. Edward W Kelly Jr and Hermann Pinkus[1] (Wayne State Univ) report experiences in treatment of 45 consecuti e patients. To rule out spontaneou egress ve changes in hypertrophic scars no keloids of less than 6 months duration were included. Many patients had had keloids for several years 1 had had large lesion for 40 years. Dosage wa 30-180 mg tetrahydroxyquinone daily

There was some fa orable influence in every case usually manifested first by a fairly prompt lessening of tension pai and pruritus Objective regression of lesions wa slow but definite In long standing keloid partial in olution continued slowly over several years. Younger lesions tended to respond m re rapidly m 3 cases involution was complete Some lesions continued to regress after withdrawal of the drug There has been no recrudescence. Follow up in some cases has been 5 years.

I several cases histopathologic change were tudied b epeated biopsy In earl er sections the collagen bundles appeared to be breaking up After treatment for 2½ years there were fewer coarse bundles, and those that remained were frayed and the fibers were wavy Fixed connective tissue cell bowed relative or actual increase in number R ticulum fibers became more vident as the collagen bundles decreased n u Metachromasia decreased under ther py wherea tain ng with the periodic acid-Sch ff proce dure ncreased, and cati g hanges in the ground ubstance. M t cells increased in mber especially those with gran les taining with periodic cid Schiff reagent. Melanocytes appeared to crease in size and seemed to have more and large dendrites.

Oral treatment f k loids with tetrahydroxyquinone lea es much to be desired It is tedious and sl w and the effect incomplete in large lesions It has however caused some regression n kelo ds of up to 40 years duration. No side effect or unt w rd reactions ha e been observed, nd the drug ha proved nontoxic m nimal even in large doses The only undesirabl reaction has been occasional local breakdown of k loid tissue accompa ed by d scharge of necrotic material. This apparently is due to softening of tis-

[1] A M A Arch Dermat 78 146 12, September 1958

sue around old devitalized collagen and is a sign of the effectiveness of treatment

Evaluation of the changes found histopathologically is difficult. The increased amount of reticulum in the treated keloid and the number and relation of the fixed tissue cells bear some similarity to conditions in fetal skin. The collagen in the regressing lesion is wavy, similar to fetal collagen. The mast cells, however, are poorly developed in fetal skin, whereas they are numerous and well granulated in the treated keloid.

Softening of treated lesions is evident on palpation and in the greater ease with which local anesthetics can be injected. The action of tetrahydroxyquinone is selective. Normal skin of persons under treatment shows none of the changes seen in the treated keloid. The exact mechanism of action of the drug is unknown. Alteration of redox potentials in the tissue is a possibility, as is action on enzyme systems.

► [A radically different and new approach to the treatment of keloids. Although this form of therapy may be prolonged, it is noteworthy that keloids of 40 years' duration responded to some extent. A trial of injection of this compound into and around the keloid is a logical next step, provided that the chemical does not produce undesirable local effects.—Ed.]

Scleroderma (Acrosclerosis).—*I. Treatment of three cases of noncalcific variety by chelation (EDTA).*—Chelate compounds are essentially co-ordinate compounds with the co-ordinate bonds arising from the sharing of an electron pair between the ion or atom of a metal and an ion or atom in the complex forming structure (ligand). The most common electron-donating or electron sharing atoms in ligand molecules are nitrogen, oxygen and sulfur. When two bonding groups are present with proper spatial orientation in a single molecule, a heterocyclic ring involving the metal ion may be formed in contrast to a complex which exists in a non-ring form. The formation of these rings is of utmost biologic importance, in that they confer behavior properties on both the chelated metal and the ligand not previously characteristic of either alone.

John G. Rukavina, Charles Mendelson, J. M. Price, R. R. Brown and S. A. M. Johnson[4] (Univ. of Wisconsin) treated 3 patients with noncalcific scleroderma (acrosclerosis) with a chelating agent, disodium ethylenediamine tetra-acetic

(4) J. Invest. Dermat. 29:273-288, October 1957

acid (Na_2EDTA) Lessened induration and shininess of the skin, particularly in the face, neck and upper arms, was definite Similar though less pronounced changes occurred in the skin of the hands. There was increased mobility of the larger joints, but joint deformities of the hands were little nfl e ced by therapy Ulcers of hands and feet healed faster with concomitant diminution of pain.

Se eral possible mechanisms of action of this drug are discussed. Though EDTA exerts its most profound effect on the richest deposit of calcium in the body in the bone it may be that ts impact on calcium in connecti e tissue (which may be abnormally laden with calcium in scleroderma) is even more significant n patients with this disease. Another possible mechanism of action of Na EDTA is mod fication of the little-understood magnesium-calcium interrelation. Finally the introduction into the body of this unnatural polyamine, polyca boxylic acid might result in changes in no way related to its chelating properties.

Experimental and speculati e evidence seems to ind cate there are several mechanisms by which a helating com pon d may influence cells sequestration of unwanted met als, emoval of metals from intact organisms reaction w th fixed intracellular metals, catalysis, tissue ligand-extraneous met l relation and impro ement of absorption Isolated examples of some of these mechanisms are known to the linician vi BAL, wherein to ic metals are removed from organisms by production of a less toxic chelate, and nickel ec ema, which a d et rich in citrus fruits leads to excretion of helate complexes.

Toxicity and side effect data in humans treated with EDTA though scarce nevertheless point to the possibility that in certain cases the treatment program may have serious consequences. Severe damage to the kidneys hemorrhagic manifestations, skin nd mucous membrane reactions, calcium embolism nausea and diarrhea ha e been reported. T xic manifestations are markedly reduced by oral adm n istration of pyridoxine. The recommended adult daily dose of Na_2EDTA is 50 mg./kg with a maximum daily dose of 5 Gm. The drug is given intravenously dissolved n 500 cc. of 5% glucose in water or normal saline. The infusion should take 4 hours. A suggested course consists in infusing the

drug for 5 days with a 2-day rest and repeating the cycle 3 times. After an interval of several weeks the course may be repeated if indicated.

II. Tryptophan metabolism before and during treatment by chelation (EDTA).—Price, Brown, Rukavina, Mendelson and Johnson[5] found 3 female patients with scleroderma to have abnormal tryptophan metabolism characterized by an abnormally large urinary excretion of kynurenine, hydroxykynurenine, kynurenic acid and Nα-acetylkynurenine. The subjects excreted normal amounts of xanthurenic acid, before and after ingestion of loading doses of l-tryptophan.

During therapy with Na EDTA the tryptophan metabolism became nearly normal in 1 patient and normal in another. Simultaneous administration of Na_2EDTA and pyridoxine considerably improved tryptophan metabolism in the subject who was the less responsive to Na_2EDTA alone. During a second course of Na_2EDTA both subjects responded as in the first trial. A third patient had normal tryptophan metabolism after treatment with Na_2EDTA or pyridoxine.

The authors explain the biochemical data on tryptophan metabolism in these 3 patients. In scleroderma there was abnormal urinary excretion of kynurenine and its metabolites after oral administration of tryptophan. Administration of pyridoxine or pyridoxine plus nicotinamide partly corrected the metabolic abnormality. The efficacy of pyridoxine plus Na_2EDTA could be explained on the basis of a decrease in tissue calcium, zinc and possibly other cations, making it possible for the metal ions normally functioning with pyridoxal phosphate to be used more advantageously. The data in the literature suggest that this metal which is unblocked for normal function may be magnesium.

► [In view of the report of Zarafonetis the abnormal tryptophan metabolism characterized by an abnormally large urinary excretion of kynurenine and related compounds is of particular interest. It is assumed that 5-hydroxytryptamine arises from the metabolic oxidation of tryptamine, the decarboxylation product of tryptophan.—Ed.]

Use of Relaxin in Treatment of Scleroderma. Louis C. Casten and Robert J. Boucek[6] (Univ. of Miami) treated 23 patients with scleroderma for 6-30 months with parenteral injections of the hormone relaxin. Relaxin in saline solution was given

(5) J. Invest. Dermat. 29:299-398, October, 195
(6) J.A.M.A. 166:319-324, Jan. 25, 1958

subcutaneously in doses of 20 mg daily for 1 2 weeks and then the slowly absorbed gelatin preparation was given in tramuscula ly 10 mg daily Conjugated estrogenic substanc (Premarin) wa administered orally in doses of 1.25 mg daily f r 2 weeks before or simultaneou with the i ti tution of relaxin therapy

Of 21 patients with a significant degree of Raynaud phenomenon, 18 noted improvement after treatment for 3-5 weeks. Improvement occurred in 14 of 18 patients with trophic lcers Complete healing of th ulcers occurred in most patients. Softening and loosening of the skin, particularly of the face and upper extremities was noted by 16 of 22 patients with generalized skin tightness. The skin of the hand and feet was not altered significantly

W thdrawal of relaxin caused a return w th n 3-10 day of Raynaud phenomenon and skin tightness Symptoms seemed to eturn in a more severe tate than before therapy b t all cases responded fa orably to subsequent relaxin dministration. Other man festations of scleroderma uch nal pulmonary myocardial failur were unaltered by relaxin treatment. To maintain the effects of th hormon t w necessary to administe it daily or e ery other day

S de effects were not of major importance. In 3 women, menorrhagia occurred during the first few men trual periods after onset of therapy T eatment was either discontinued o the dose educed duri g the menorrhagia. One patient had distressing local reactions to the injections and refused fur the t eatment. Th ee noted weakness and n 1 this symptom w s se ere that treatment wa discontinued.

R laxi fluences connective tissu ther than that found n d aro d the genital tract The response of the aso-spa t feat re of the d sease Raynaud s phenomenon to the horm ne uggests that a asodilator ffect may be operating The hara ter f thi reaction is u known but may be re lated to the action of laxin on the mast cell. Response of trophic ulceration may be lated to depolymerization of the grou d-substance connecti tissue which m ght permit more rapid diff sion f ubstances from the ascula tree Further kin n trition may be improved b a ncrease of it scula supply ulting from amelioration of vaso-pa m Loosening f the kin of patient w th scleroderma

may be related to the action of relaxin on the collagen fiber

► [On the basis of personal communications from others, it is our impression that relaxin is useful principally to promote healing of the ulcers in acrosclerosis but that it has very little if any effect on the sclerodermatous cutaneous changes.—Eds.]

Intravenous Procaine in Management of Some Cutaneous Manifestations of Collagen Diseases was used by Joseph Farrington[7] (Jacksonville, Fla.). Each patient was hospitalized, then prepared by administration of Seconal 0.1 Gm. orally 20 minutes before starting intravenous therapy. The initial dose consisted of 500 cc. of 0.1% procaine in normal saline or 5% glucose solution. If there were no untoward reactions, the patient was given 1,000 cc. once a day for the next 6 days at 45 drops/minute. Such courses were repeated at intervals of 6 weeks until optimum improvement was obtained. If there was no additional improvement after the third course, therapy was discontinued. The maximum number of courses given any one patient was 12. No serious side effects were observed.

Of 71 patients with scleroderma of all types who were treated, in about half the condition was acroscleroderma or generalized. Improvement varied in degree but seemed permanent. There was softening of the skin in most; soreness, stiffness and swelling of the joints improved. Raynaud phenomenon present in 8 patients with acroscleroderma responded dramatically in 6. The sharp borders of localized scleroderma usually at the end of 6 weeks would begin to blend imperceptibly into the surrounding skin with gradual disappearance of the lilac halo. Of 71 patients with all types of scleroderma encountered over 7 years, only 2 died. These were young women who were moribund before receiving intravenous procaine. In 3 patients with dermatomyositis and severe Raynaud's phenomenon, vasomotor symptoms were relieved by procaine treatment.

The author had hoped that by relieving the confinement of a "hide-bound" epidermis in patients with scleroderma or dermatomyositis the underlying musculature would over a period regain its normal size and development. However, muscular atrophy persisted, apparently unchanged long after the overlying skin became soft and pliable.

► [Any method which does not produce serious side effects but yet may

(7) South. M. J. 51:1426-1431, November, 1958.

be of aid to some patients is worthy of trial in scleroderma where ordinarily so little can be done to help.—Ed.]

Treatment of Psoriasis with Riboflavin. Bencel L. Schiff and Arthur B. Kern[a] (Boston Univ.) treated 90 patients who had chronic psoriasis. Weekly injections of 1 cc. of aqueous solution containing 50 mg. riboflavin 5-phosphate sodium (equivalent to 35 mg. riboflavin) was given to 77 patients fo 1-4 months. 40 of these also received riboflavin orally 7.5 mg. 3 times da ly. Thirteen patients received 1 cc. riboflavin solution intramuscularly daily for 4 months.

Of the 90 patients 33 showed some improvement. Relief from itching was noted n some of the 57 who showed no objective improvement. Patients who received daily inject ons showed no greater benefit than those who received weekly injections. The addition of oral treatment failed to ha e any demonstrable ffect. The uthors conclude that ribofla in has little value n treating psoriasis.

► [W agree.—Ed.]

Sulfonylurea Derivatives in Treatment of Psoriasis Vulgaris. Preliminary Report. G. Kabelitz and W. Kappel[a] changed the treatment in 2 d bet pat ent w th psoriasis from insulin to Artosin, a benzinesulfonylurea derivative. After 3-4 weeks treatment with 0.5-1 Gm. Artosin daily the psoriasis improved considerably. Trial of Art sin in 25 more psoriatic patients without diabetes led to healing or great improvement in 1/ during a follow-up of 6-12 months. Only far-advanced and extensi e psoriasis responded to Artosi Response was independent of ge, sex or age at onset of the disease. A hypoglycemic eaction which required discontinuance f the medication occurred only once. In mild eaction temporary eduction of the dose ufficed.

The effective dose of Artosin is 0.5-1 Gm. daily n 2 divided doses. Improvement can be expected in 15-20 days. Med catio mu t be continued until cure is effected or there is great improvement. Thereafter a smaller maintenance dose is d sable. A relapse calls for new course of Artosin. The mode f action of the drug in psoriasis is unknown.

T eatment of Psoriasis with Folic Acid Antagonists. Walter F. Edmundson and William B. Guy (Pittsburgh) treated 6_ patients with moderate to severe psoriasis with

A.M.A. Arch. Dermat. 78:643, November, 1958.
Deutsche med. Wchnschr. 83:1146, July 4, 1958.
A.M.A. Arch. Dermat. 7 : 200-203, August, 58.

aminopterin amethopterin or both The dosage of aminopterin was 0.5 mg daily for 6 days withdrawal for 3 days and 0.5 mg daily for 6 days Amethopterin was given in the same manner in dosage of 2.5 mg daily for a total of 30 mg in 12 doses. Some patients were treated further with 0.5 mg aminopterin or 2.5 mg amethopterin daily for 9 days administered 3 weeks after the original course Repetition of a course of 12 doses was not prescribed until 3 or more months after the original therapy The rest periods probably reduced accumulative toxic effects of the drugs In this series mild toxic effects were rarely observed and there were no serious untoward reaction

Aminopterin was given to 32 patients 17 received amethopterin and 13 received both drugs Aminopterin in doses of 0.5 mg gave almost identical clinical results as amethopterin in 2.5 mg doses Of those patients who received only one of the drugs 75% had over 50% improvement at the time of the last observation period which in several cases was more than 6 months after treatment Of the 13 patients who received both drugs 11 maintained more than 50% improvement until the last observation date

The relatively low and almost nontoxic dosage schedule used appears to be practical for treatment of moderately severe or severe cases of psoriasis although the clinician must be alert to toxic effects and drug idiosyncrasy which may occur in any patient taking folic acid antagonists Because of the toxic effect on fetal tissue it is probably best not to give the drug to women during the childbearing age

► [One can draw the conclusion from the article that, as reported by Rees, Bennett and Bostick, aminopterin and amethopterin are beneficial in many cases of psoriasis and that they do not produce immediate toxic effect of consequence in the conservative doses used. As has been pointed out on many occasions in the past, patients receiving these folic acid antagonists should have careful medical follow-up including repeated blood counts.

Besides the folic acid antagonists, most patients in this study used topically a mercury soap or ointment and received injections of 1,000 μg vitamin B_{12} or 35 mg riboflavin every week for about 3 months after their course of treatment. These were given to provide post-treatment observation.—Ed.]

Effect of Cycloserine on Skin Tuberculosis: Preliminary Report is made by Juvenal Esteve (Univ. of Lisbon). Cycloserine is a new wide-spectrum antibiotic which has [illegible]

(2) [illegible] 8 494-496, November 195

tained from various streptomyces species. It was first used in patients who w re resistant to streptomycin and isoniazid.

The author tried cycloserine in 22 patients with skin tuberculosis (2 had lupus vulgaris and 20 erythema induratum Bazin and papulonecrotic tuberculids) The daily adm n s tration of 0.75-1 Gm led to clearing of tuberculid type skin changes in 8-60 days in 18 patients who tolerated the drug well In 2, the drug had to be discontinued right at the beginn g because of severe de effects. In 4 elapses occurred between 2 and 8 week

The therapeut c effect wa relat ely un form quick and independent of pr viously gi en treatment The blood sedimentatio rat n nall became normal when the patient m pr ed clinically In lupu ulgaris, cycloserine given in the bo amo nt for 2 month did not hav any cl nical or h tologic effect on the granuloma. The discrepancy between the good e-ult m patient with tuberculid and the poor e ult those with lupus vulgari if confirmed by further tud es m ght throw some l ght on the possible organotrops mode of ction f cycloserine.

Treatment of Leprosy with Cycloserine, an antibiotic obta ed f m ultu es of St eptomyces chidaceu garyphalu nd la endula and also ynthetically was assayed in 10 pat ent by V P rdo Castello (Um of H vana) The drug p e iously wa used to treat tuberculos Some of the pa t ent had had no pr viou treatment and other had been t eated f rying period with diam nod phenylsulfones with sat fact ry ult r no effect

The dosage f d-cy loserin (d-4-amino-3-isoxaz lid none) sed wa 500-1,000 mg /day n tablet of 250 mg taken with gla of water Th larger doses of 1 Gm produced t times g tn testinal d general symptoms, and hence were re l ced t r 3 tablet da ly (500-750 mg) Tolerance n all ses wa g l w thout renal, hepatic or hematologic com pl cations. The pat ent ema ned good general health, a l laborat ry t t terial pres ure nd psych c tate were normal

The res lt f treatment, which la ted from 3 to 15 months were f vor ble w th slow progres clin cal improvement utaneous and mucosal lesions similar to that seen with

Rev Sov cubana dermat 28, March, 58

aminopterin amethopterin or both The dosage of aminopterin was 0.5 mg daily for 6 days withdrawal for 3 days and 0 5 mg daily for 6 days Amethopterin was given in the same manner in dosage of 2 5 mg daily for a total of 30 mg in 12 doses. Some patients were *treated further with 0 5 mg aminopterin or 2 5 mg* amethopterin daily for 9 day administered 3 weeks after the original course Repetition of a course of 12 doses was not prescribed until 3 or more month after the original therapy The rest periods probably reduced ac cumulative toxic effects of the drugs In this serie mild toxic effects were rarely observed and there were no seriou untoward reactions

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Effect of Cycloserine on Skin Tuberculosis Preliminary Report is made by Juvenal Esteves[2] (L nic f l t b m) Cy closerine is a new wide-spectrum antibiotic whi h

(2) Hospital 8 491-496, November 1957

romas. This lighter appearance signifies beginn ng resorption Simultaneously hypertrophy of the leprosy cells can be observed which increase their volume two to three times without re ealing any structural changes.

With progressive treatment, early in the 2d year when the drug effect on the leprosy bacilli becomes more ntensive, a large number of Virchow cells show various changes the meshwork of the intraprotoplasmatic reticulum begins to tear and coalesce Later these ntracellular changes affect more and more V rchow cells.

The resorptive processes are not always uniform often there re zones with far-advanced healing besides areas of uncha ged nfiltrations The resorption usually proceeds from deep to superficial areas beginning in the subcutis.

In the course of lepromatous leprosy the lymph nodes are con ta tly involved the inguinal, femoral and cervical nodes are most commonly invol ed. The successive histologic changes in the lymph nodes under sulfone treatment are s milar to those seen n the skin

Most of the leprosy bacilli are found n the histiocytic cells. Ins de these "leprosy cells (or Virchow cells) the bacilli m ltiply igorously fill th entire cell and remain there for long tim During the first months of sulfone treatment, en before hi tologi changes become apparent, the bacteria become fewer and appear granular Toward the end of the 2d treatment year all the bacilli not only appear granular but change their characteristi pattern of grouping Simultaneou with the advanced ellular destruction, the bacilli disappear f om the ell by dissolution Some still remain inside the ll whereas others are expelled nto the surrounding tissues where they appear as isolated granular rods W th progressi e treatment, these rods disi tegrate into masses of f ch moph l e en cyanophil granules. Leprosy bacilli es t treatment longer in the ly mph nodes than in the sk n Theref re th terilization of the lymph nodes can be con idered the most mportant test of cure

Sulfamethoxypyridazine in Dermatitis Herpetiformis. J Jefferson[4] (Belfast) eports satisfactory esponse in the treatment of 12 patients. One patient had a seve e bullous eruption and 4 had the juvenile type of dermatitis herpeti-

Brit. M. J. 2 209 21 July 24, 958.

sulfone treatment. There was little change in microscopic findings despite intense and prolonged treatment Acid fast bacilli of Hansen were investigated weekly at first and later every 2 weeks or monthly these were demonstrable in all cases but with some favorable changes i e. signs of degeneration in both cutaneous and nasal mucosal lesions

Clinically the improvement was as marked as that with diaminodiphenylsulfones *Lepromas softened, faded and were absorbed* infiltrative lesions of the palatal and laryngeal mucosa were reduced within a few weeks and finally flattened into red or reddish macular lesions and diffuse cutaneous infiltrations were reduced in size and remained as reddish erythemas which later faded and disappeared slowly *In 2 cases in which diaminodiphenylsulfone apparently* yielded no benefit cycloserine gave favorable results clinically permitting 1 patient to resume his professional activities without any sign of the disease. Treatment had to be suspended in 1 patient because of psychic disturbances which were probably not caused by the medication since psychiatric investigation revealed a mentally disturbed individual

Cycloserine is an excellent addition to antileprous therapy and deserves a large scale trial in doses not exceeding 750-1 000 mg/day

Histologic and Bacteriologic Changes in Lepromatous Leprosy after Treatment with Diaminodiphenylsulfone (Sulfone Parent Substance) St G Nicolau and [illegible] [4] (Therapeutic Inst of [illegible] charest) treated [illegible] 120 patients who [illegible] e [illegible]iologic and bacteriologic c[illegible]nges which took place in the slowly healing and finally disappearing skin lesions were [illegible]tudied The histologic changes began during the 2d month but became pronounced during the 4th and 5th months of treatment. Thereafter a slowly progressive but steady *resorption* of the lepromatous changes could be *observed* C[illegible]*mplete resorption* took about 2½ 3 years or more

Biopsy specimens of lepromas taken at regular interval during treatment showed first a lighter appearance [illegible]f part or all the infiltration—*in striking* contra[illegible]t t[illegible] untreated lep-

(4) Arch. klin. u. exper Dermat. 207 486-498 1958

high inherent error Among the considerations that deter min a patient s answers to questions in complex situations re (1) the actual pharmacologic effect of the agent under test (2) ignorance or disbelief that a placebo was or might ha e been used (3) dose of the active agent (4) ancillary cues uch a gastric irritation to the active agents (5) spec ficity fficacy and conspicuousness of response to the active agent (6) problems of semantic interpretation of both questions and answers (7) nature of the questions asked, w th particula regard to a tendency to suggest or to inhibit a particular an wer (8) efficacy of concurrent therapeutic agents or other changes n the patient s environment includ ing passage of time nd (9) the base line against which the patient mu t make comparison.

► [This study seems to prove principally tw items (1) "the high inherent testimonial error" as it is called by the authors, which must be reckoned with in such studies, and (2) the failur of 8-methoxypsoralen (M louxe) to significantly chang the sunburn and sun-tan reactions of the subjects studied under the conditions of the tests This drug was e leased with the laim that in doses of 20 mg it protects against sunburn and increases skin pigmentation The authors administered 10-20 mg with ery unconvincing results Therefore, w feel that t present such claims are unwarranted It seems to us that from public health viewpoint der matologists should explain why the public should not sun-bathe and sun tan excessively thus discouraging overexposure The promotion of Melox ine sunburn prevention and sun-tanning agent does exactly the oppo site it encourages even more sun exposure—Eds]

Effect of Diphemanil Methylsulfate (Prantal*) on Hyper hidrosis of ary ng degree in 51 patients was investigated by N rman Orentrei h and Charles Robert Rein[1] (New York U Post-Grad. Med. School a d Ski and Cancer Unit) Schedules rying from 50 to 400 mg 1-4 times daily were sed A th ffect wer determined, patients adjusted the dosage schedule to indi idual needs. The effect of n adequat dose of d phemanil methylsulf te w apparent in 30 m tes and la ted 4-5 hours th re were no permanent ef fect Generally the higher th dose, the mor effecti e t wa for hyperhidros and the mor ide ffects it produced.

Of the 51 patient response was excellent in 13 good in 28 a l moderate n 7 The a erage dose required for good results was 200 mg every 4-6 hours. Xerostomia occurred in 1 patient t was minimal n 4 mild in 8, moderate n 5 nd severe in 4 Othe s d effects noted were bitter ta te tin

[1] A.M.A. Arch. Dermat. 76:2 45 December 1957

formis. One adult and 3 children remained well after cessation of treatment.

Most adult patients received 3 or 4 sulfamethoxypyridazine tablets daily for 1 to several weeks until the eruption cleared. Maintenance dose was 1 or 2 tablets daily in most, though some patients required 3 or even 4 tablets to prevent recurrence of lesions. Dosages were lower in children.

In view of the variable course of dermatitis herpetiformis and the possibility of spontaneous remissions, it is difficult to assess the results of treatment. All these patients, however, responded immediately. In 2 cases treatment was interrupted when supplies were temporarily held up. In each, the eruption promptly recurred and rapidly disappeared when treatment was resumed.

Toxic symptoms were almost entirely absent despite the comparatively large doses of sulfamethoxypyridazine. One patient had what appeared to be genuine rubella and continued treatment without ill effect. Another had dizziness and headache but was able to continue the necessary dosage without further reactions. One patient has been taking 4 tablets daily for over a year without side effects. Blood count and urine have remained normal.

► [The incidence of drug eruptions among patients treated with sulfamethoxypyridazine (Kynex) has been rather high, and some have been serious (this YEAR BOOK, p. 182). This would seem to preclude wide use of the drug in a chronic disease such as dermatitis herpetiformis.—Ed.]

Effects of Oral Methoxsalen (8-Methoxypsoralen) on Sunburn and Sun Tan: Blind Clinical Trial. Farrington Daniel, Jr., Carl E. Hopkins and Thomas B. Fitzpatrick[6] (Univ. of Oregon) report that a double blind controlled study of reactions of 106 patients using methoxsalen (10-20 mg. daily) and an identical placebo failed to show that these patients could discriminate between lactose placebo and methoxsalen as to sunburning and tanning effects. A significant relation was found between the patients' statements of their usual tendency to sunburn and their claimed protection from sunburn while using the blind placebo.

Since methoxsalen is a known potent photodynamic agent, the point of the authors' study is not that patients are reacting falsely to an inactive agent but that testimonial data have

(6) A.M.A. Arch. Dermat. 77:503-507, May, 19

In all patients, besides the reserpine, fomentations of aluminum subacetate (1%) and an ointment of equal parts zinc oxide, talc, glycerin and distilled water were given. As controls, some patients received identical local medication and antihistamines. Comparative studies showed definite control of pruritus in those treated with reserpine control was inconsistent in those treated with antihistamines. No side effects were noted w th reserpine except in 1 patient who had headaches on 0.75 mg daily The satisfactory tolerance may be attributed t the low doses used. The average of 0.375 mg was much less than others have used in treatment of other dermatoses (to 4 mg)

On the basis of the favorable results obtained in this series, eserpine deserves wider trial n treatment of eczema of the legs due to vascular insufficiency

► [It is difficult to assess accurately these results obtained with reserpine in eczema of the legs since no placebo medication was given to the subjects who were benefited However there are several possible explanations as to how reduction in itching may occur under reserpine medication (1) the general tranquilizing effect (2) central nervous system effect as on the diencephalon (3) sympatholytic, lowering of blood pressure or other pharmacologic actions, and (4) an effect on the mast cells in the skin The last mentioned possibility must be considered in view of the peculiar effects observed by Bernard, Pelzig and the senior editor in 3 patients ith urticaria pigmentosa who received reserpine—Eds]

Treatment of Chromoblastomycosis with Calciferol is discussed by Clovis Bopp. Surgical or electrosurgical treatment of chromoblast mycosi s often followed by relapse o the appearance of metastatic lesions. An apparent explanation is that surgical procedures often open the fibrous barrier in the deep corium which tends to keep the fungus localized to the upper corium and epidermis. The only exception t this is the method of Farina, in which a wide and deep excisio down to the aponeurosis is followed by skin grafts. However th s method is only practicable for lesions f l m ted tent.

T eatment with calciferol combined with iodides may be con dered the first rational treatment of this d sorder The uthor has used three plans of treatment which were developed cces l a xperience demonstrated the disadvantages of previous plans Under the first plan, oral calciferol w gi en n 600,000 unit doses every other day for 30-80

(9) Ofs Gerf Livraria do Globo, Porto Alegre, Brasil, 195

gling of the tongue, gas in the stomach nausea and dry nose No difficulties with accommodation were noted.

Determinations of the diphemanil methylsulfate-methantheline (Banthine®) antisweating pharmacologic ratio were made in 12 patients The weight for weight ratio was about 4 1 (200 mg diphemanil being equal to 50 mg methantheline) in 6 patients and over 2 1 in the other 6. Xerostomia occurred in 75% of the patients taking methantheline.

A review of the literature revealed that some failures to achieve uniform results with the quaternary amines were due to inadequate dosage uncontrolled variations in dosage schedules and lack of provision for variations in patients response to these drugs

► [We also have had favorable experiences with diphemanil methylsulfate in some patients, but in others the side effect with any anticholinergic drug are so disagreeable that the patient prefers the hyperhidrosis —Ed]

Antipruriginous Effect of Reserpine in Eczema of Legs was studied in 23 patients by David Grinspan and Jorge Mu-hafra[8] (Buenos Aires) Eczema of the legs in patients with venous insufficiency is difficult to treat and frequently recurs Although appropriate local treatment often produces improvement with decrease in pruritus this may not disappear entirely A vicious circle is then established persistence of pruritus and consequent scratching exacerbates the eczema which in turn increases itching Under such conditions antihistamines and older antipruriginous remedies (calcium magnesium hyposulfite peptone etc) usually fail Barbiturates and other sedatives carry the risk of sensitization and drug allergy which would make the dermatosis worse. Further they have no significant effect Corticoids and ACTH are expensive and require special caution if used for some time

In the 23 patient (16 women) treated with reserpine eczema of the legs was secondary t en us in ufficiency although actually the eczema wa of microbial origin The amount used varied between 0.25 mg in 2 doses and 0.75 mg in 3 doses In most 3 doses f 0.125 mg (0.375 mg daily) were sufficient. Results with respect to pruritus were excellent in 14 patients (10 women) and good in 9 ((w men) In 17 the effect was immediate, and in 6 relief appeared after 5-10 days Maximum duration of treatment wa 45 day

(8) Arch. urug. med. 7:347-372, December 195

Calciferol seem only to stimulate the same defense reaction which the host normally de elops to circumscribe and dominate the invadi g organism. Without showing apparent fungistatic r fungicidal ffect calciferol enhances the prol f eration of fibrous tissue and reduces the cellular infiltra tion It probably has the same biochemical action m chromoblа tomycos that Charpy has described in lupus ulgari nam ly production of ti ue cidosi and enhancement f the hydrolytic action of alkaline phosphatase with l'beration of phosphoric io s. Others hav hown that tis ue acidifica t n elicit connecti e tissue prol feration.

Trial of Chloroquine in Treatment of Lichen Planus. Veikk Pirila and S rkka Helanen (Univ of Hel inki) treated 35 patient Duration of the d sease before treatment wa les than 3 month n 12 cases 3-6 months in 14 and more than 6 m nth n 9 The u ual dosage was 0 250 Gm chlоroq ine daily but 11 patients received 0.5 Gm dail du ing part f the treatment period Duration of treatment wa 1 3 mo th m 15 ases, 3-6 months in 13 and o e 6 months 7 s d effect occurred n 9 patient One patient exhibited a generali ed erythroderma after 1 month of treatment 1 pat ent had m ld leukopenia a d the other had mild, tran ent mpt m ncluding nausea, insomnia, tired es ertige n l nal di turbances

After 6 mo th t e tment 21 patient (60%) still had a t l n The corresponding figure n Samman cases f nt eated lichen pla u w 43% Only 3 of the present 35 patient were fr from l ion after total duration of the disease f 6 m th (including the period before and dur g treatment) nd n 22 pat ent (63%) ct e lesions were t ll present fter the disease had been present 12 month Among Samma patient 27 4 till had lesio 12 months fte onset

Thu the cou se f l he planu wa more prolonged in patient t eated w th hloroqu e than n untreated pa t ent Though the d fferenc m be in ignificant, t i lent that hloroquin ha l ttle no ben ficial effect n th se f the d sease

( )This negative finding is presented her since it may prevent others f m using this form of treatment in lichen planus l idespread, symp

doses Occasionally the course was repeated once or twice With this method some patients relapsed after initial improvement and many exhibited symptoms of overdosage. In the second plan calciferol was given on alternate days for 2-6 weeks and then once a week for 30-40 doses No significant toxic effects were noted The third plan called for administration of calciferol in doses of 600 000 units weekly for 15 25 weeks No toxic effects were observed and the lesions flattened out more rapidly than with the other plans.

In all three plans besides calciferol each patient received 1 3 Gm potassium or sodium iodide. Compresses of Alibour or Thierch solution were also applied When exudation diminished most of the patients used Unna s zinc gelatin boot for 1 2 weeks

Of 14 patients treated by the first method 2 showed histologic cures in an average of 9 months and 8 showed clinical cures in an average of 7 months Four showed substantial clinical improvement and are still under observation after an average of 17 months Of 5 patient treated according to the second plan 1 was cured histologically after 6 months, 3 were cured clinically in an average of 5 months and 1 has shown significant improvement after 6 months. Of 5 patients treated by the third method 1 was a new patient and 4 had relapses following treatment by the first plan Two of the 5 were cured histologically in an average of 3 month 2 were clinically cured in an average of 3 months and 1 showed significant improvement after 2 months at which time he abandoned treatment

The host reaction to the fungi in chromoblastomycosis features several steps (1) development of dermal microabscesses containing numerous fungi (2) formation of dermo epidermal fistulous openings making possible the discharge of these suppurative foci to the exterior (3) development of a band of cornification in the malpighian layer giving rise to horn pearls containing cellular debris and fungi (4) granulomatous reaction in the dermis with formation of epithelioid nodules and destruction of encircled fungi and (5) formation of a fibrous barrier in the deep corium limiting the cellular infiltration while newly formed bundles of connective tissue cross the upper dermis in all directions tending to replace the infiltrate with scar tissue

definite b t limited reduction in rhus sensitivity may be at tained by oral or intramuscular administration of rhus aller gens With rhus oleorea n, maximum hyposensitization i obtained with about 2,000-2,500 mg intramuscularly and 2,500-3,000 mg orally With the pure but less potent penta decylcatechol, this state is reached with about 2,500-3,000 mg intramuscularly and 3,500-4,000 mg orally

Hyposensitization occurs in a definite pattern revealed by quantitatn patch tests. The reaction to the highest dilution declines first. Only the end portion of the dosage-response curve is notably affected A 100-fold decrease in titer is rare A given fraction of the original sens tivity may be abolished but no more regardless of the height of the total dose or the initial degree of sensitivity

Varion sy temic and mucocutaneous side effects may appear i the course of hyposensitization They are attributa ble so far as present understandi g goes entirely to allergic reactions The main signs and symptom are mucocutane- n prurit an flares of healed sites rashes dyshidros and urticaria. Sy temic reactions n this study were never met w th conserv ti oral prophylaxi Such reactions to ntramuscula treatment were mild a d nfrequent with mservat prophylaxi but severe and frightening with mor gorous t eatment Sy temic reactions included fev r grippelik syndromes muscl a hea, asthenia, meningismus bout f coughing and wheezing and headaches No anaphy la t d eactions were observed

The blood cell wh h most sensiti ely reflects the impact t rall or pa enterally adm tered rhu ant gens in sen sit ed per-son the eosinophil. Eos noph lia s an nev ta ble de lopment in e ery in tan e of cl nical sen tizatio whether m ld or trong in which large quantities of allergen ha been gi en especially ntramuscularly With conserva t oral prophyla s, eosinophilia is less ntense and often absent Leukocytos s, with whit blood cell counts of 10,000-24,000 often ccompan es intense eosinophilia and is in pro- p rtion to t With conserv ti e oral o ntramuscular penta decylcatechol prophylaxi other changes in the perip h ral blood n common

H posensitization is not eas ly achieved in allergic con tact dermatit One is co fronted with the problem of gi

tomatic cases of lichen planus, triamcinolone or other corticosteroids may be worth a therapeutic trial.—Eds.]

Vitamin B_{12} in Treatment of Congenital Ichthyosiform Erythroderma. A. Lodin, H. Gentele and B. Lagerholm[2] (Karolinska Hosp., Stockholm) treated 5 patients with congenital ichthyosiform erythroderma with extremely large doses of vitamin B_{12} (1,000-6,000 µg. daily) intramuscularly combined with vitamin C (up to 1,500 mg. daily) orally. No other treatment was given concurrently. Spontaneous remissions had not occurred previously in any patient. Pronounced improvement was observed in all. In 2 patients, improvement did not begin until treatment had been given 2-3 weeks. In 2 others, improvement occurred with doses of 1,000 µg. daily, but the healing process ceased after several weeks of therapy. Dosage was then increased in increments of 1,000-2,000 µg. to a maximum of 6,000 µg. daily. With each increase in dosage, improvement was again noted. When treatment with vitamin B_{12} was stopped, exacerbations occurred within a week or so. The healing process was similar in all cases. The first sign of improvement was detachment of the scales marginally. Desquamation then occurred and the skin became paler and softer. No side effects were observed with the massive dosage of vitamin B_{12} used.

According to various investigators, one function of ascorbic acid is that it plays a significant part in the conversion of folic acid to citrovorum factor. Though the interaction of vitamin B_{12} and folic acid in cell metabolism and maturation is not completely understood, some authors believe that vitamin B_{12} also participates in the formation of citrovorum factor from folic acid. Vitamin B_{12}, folic acid and citrovorum factor all take part in normal cell maturation. Accordingly, the authors administered a large adjuvant dose of vitamin C in the belief that it might reinforce the effect of vitamin B_{12}.

► [In the 1 case in which this treatment was used by D. H. Gordon at the New York Skin and Cancer Unit, similar results were achieved. Improvement was noted up to a point, beyond which there was no further progress despite continuation of therapy.—Eds.]

Hyposensitization against Rhus Dermatitis is discussed by Albert M. Kligman[3] (Univ. of Pennsylvania). During 3 years many different schemes of hyposensitization were tried; more than 2,000 subjects participated in the study. A

(2) Acta dermat.-venereol. 38:31-47, 1958.
(3) A.M.A. Arch. Dermat. 78:47-72, July, 1958.

lyzed by P. de Graciansky and Ch. Grupper[4] (Saint Louis Hosp. Paris). Five had sero-negative primary syphilis, 29 sero-positive primary syphilis, 51 secondary syphilis (3 reinfection), 8 gummas, 9 tabes with or without meningeal reactions (arthropathy), 2 aortitis, 3 gumma 1 and optic neuritis 1, 5 aortic syphilis (? with aneurysm), 3 serologic syphilis discovered during pregnancy, 2 pure serologic syphilis, 4 late congenital with interstitial keratitis and 4 known sensitivity to penicillin.

At the beginning of this series cortisone was used intramuscularly or by mouth for 5 days, then 5-8 days (exceptionally 30 days) 100 mg/day. In 21 cases hydrocortisone 100-120 mg/day was given 5-6 days, sometimes for 15 days. In 2 cases perfusions of ACTH 25 mg in 500 cc glucose saline solution were tried. Local corticotherapy was used as subconjunctival instillations or injection in interstitial keratitis and intra-articular injections of 1.5 cc hydrocortisone were given in arthropathic tabes. In the last 30 cases delta 1 dehydrocortisone 30 mg/day was given for 6 days. In the technic currently used, the single penicillin injection is given the 4th or 5th day of the cortisone course.

Cortisone prevents or decreases in most instances the Herxheimer reaction both in acute and chronic cases. Only 6% of the patients in this series had temperatures of 102.2-104 F. following penicillin injection, as contrasted with 50-80% usually reported when cortisone is not used.

Clinical manifestations of syphilis, including chancre, secondary syphilid, cutaneous and mucous gummas, subjective symptoms due to neurologic involvement and interstitial keratitis are modified by cortisone. Improvement varies with stage and severity of the lesion. Cortisone significantly reduces pathologic evidence of activity with diminution or disappearance of treponema, decreased concentration of reagin in primary and secondary syphilis and in tertiary cases with clinical manifestations, and lessening of abnormal findings in cerebrospinal fluid. Conversely there is no change in reagin concentration when it is low in the so-called specific serologic tests. Cortisone does not diminish treponema sensitivity to penicillin nor is the usual course of syphilis after penicillin treatment altered. Cortisone is useful as an adju-

[4] Rev. Prat., études clin. et biol. 2 579 584, 1957

ing a large amount of allergen safely. Intramuscular prophylaxis is not feasible in clinical practice. Too many injections are required and, even with conservative dosage, adverse reactions are too numerous and severe. Oral prophylaxis is preferable. Doses can be advanced slowly by small increments. Signs of intolerance can be recognized early and intercepted. Pentadecylcatechol is theoretically advantageous because of its purity and stability. Unfortunately, its synthesis is somewhat costly and it will not be available in the immediate future.

The usual initial dose of pentadecylcatechol is 1 drop of a 10% alcoholic solution daily for a week. This is gradually increased; 2 drops are given daily the 2d week, etc. With oral prophylaxis, skin rashes and pruritus are the symptoms which most often prevent advancement of the doses in the prescribed manner. Some patients react even to 1 or 2 drops. This barrier can generally be overcome by daily administration of 50-100 mg. cortisone acetate or its equivalent, depending on the severity of the reaction. Even with cortisone the dosage must be cautious and personally regulated.

At present nothing is known about the mechanism of hyposensitization. Presumably the allergen in some way combines with and binds antibody so that it is no longer available for reaction with allergen. Hyposensitization is temporary. It begins to wane after a few weeks. The original sensitivity is gradually regained within 0.5-10 months, occasionally longer. Maintenance dosage was incompletely studied. Five drops of 10% alcoholic solution of pentadecylcatechol daily by mouth was adequate maintenance in 20 subjects. Lower amounts were not investigated.

► [In this study Kligman confirms much of what was previously known besides revealing some interesting new data regarding hyposensitization to poison ivy. The relatively small differences in the quantities of allergen necessary for hyposensitization by the oral method (2,500-3,000 mg.) and intramuscular method (1,000-2,500 mg.) are notable, as are the hematologic changes (eosinophil and total leukocyte counts).

Because it is stable and pure, pentadecylcatechol in some ways would be advantageous for hyposensitization procedures. However, one must ask whether this very stability is not also a drawback, because it is likely to make this compound immunologically nonaggressive as compared with the less stable unsaturated compounds among the poison ivy allergens.—Eds.]

Cortisone and Syphilis: Results of Corticotherapy Preceding Course of Penicillin in 120 Cases of Syphilis were ana

sing agents in the treatment of syphilis but further evaluation seems indicated before recommendation of their widespread use in treating this disease. Tetracycline and synnematin B have recently been used successfully in treating a few cases of early syphilis.

► [For general use, penicillin remains the therapeutic agent of choice in syphilis. However because of the increasing incidence of severe and dangerous reactions due to penicillin sensitivity it is important to know what other antisyphilitic antibiotics are available. In these times when such a large proportion of the population has been previously exposed to penicillin, it is wise to have at hand those materials which will be needed should the patient have systemic (anaphylactoid) reaction following penicillin injection.—Eds.]

C. Physical Therapy

Radiation Protection in Dermatology Anthony Domonkos and Gordon H Cameron (New York) studied for several years the amount of radiation to which dermatologists and their assistants were exposed in active private practice The study was done in an office with 3 identical x ray machines of modern design a contact x ray apparatus 300 mg radium, and thorium X in alcohol solution.

The inherent filtration of x ray tubes and their housings was equivalent to approximately 1 mm Al. The machines operated at 100 kv 7 ma target skin distance 30 cm. and half value layer 1.4 mm Al The inherent filtration of the contact x ray tube and its housing was 0.15 mm. Al and the machine operated at 45 kv 2 ma half value layer 0.3 mm. Al and target-skin distance 1.8 cm. The radium supply was stored in a conventional safe in a cabinet with lead walls 3½ in. thick. Thorium X was used for 2 days every week, an average of 1,500 μc being used weekly

Film badges, worn intermittently by all office personnel were changed at weekly intervals. A total of 444 film badges was used In addition 2 pocket dosimeters were used by those especially concerned with radium therapy On the basis of measured scattered radiation from roentgen apparatus and direct radiation received from radium and thorium X correlated with amounts received by dermatologists and their personnel, it was found that they were protected well

(A.M.A. Arch. Derm. 7 ... , December 1957

vant to relieve sharp pains and visceral crises of tabes arthropathies and interstitial keratitis When cortisone is given penicillin is tolerated better by allergic subjects and pregnant women and in patients with aortic and neurologic syphilis

Although some facts such as morphologic change in the treponema under the influence of cortisone alone their diminution and their earlier disappearance (as compared with controls) in primary or secondary lesions suggests a possible direct effect on the organisms the principal therapeutic effects of cortisone are attributed to changes in the host. Effect on rate of circulating antibodies changes in specific infiltration and changes in cerebrospinal fluid reactions all favor this hypothesis The anti inflammatory and antithermic effect of cortisone accounts for the favorable effect in preventing febrile reactions Another mechanism suggested by the authors is that corticotherapy affects favorably the concentration of penicillin in the plasma. The question is also raised as to whether cortisone may increase the treponemicidal power of the penicillin

Treatment of Syphilis with Antibiotics Other than Penicillin. With growing frequency the physician faces the problem of choosing a therapeutic agent for patients with syphilis who are sensitive to penicillin The choice is between a return to the difficulties and dangers of treatment with arsenic and bismuth and use of some other antibiotic with treponemicidal properties Sidney Olansky (Duke Univ) and Warfield Garson[8] (Univ of North Carolina) reviewed the literature concerned with the treatment of syphilis with antibiotics other than penicillin

Streptomycin was the first of the newer antibiotic to be used, but it gained little favor because the large doses necessary to control syphilis were too toxic Chlortetracycline chloramphenicol and possibly oxytetracycline have been successfully used in enough patients to demonstrate their effectiveness in early syphilis benign late cutaneous syphilis, neurosyphilis and prenatal syphilis There is little reason to believe that these three antibiotics would not be effective in latent syphilis and cardiovascular syphilis in adequate dosage. Carbomycin and erythromycin appear to be p r m

(8) A.M.A. Arch. Dermat. 77:640-650, June, 1958

, cl nical study and to check on the clin cal findings the uthors also made measurements on an untempered pressed w od phantom. Doses and technics in irradiating the phantom paralleled those used in treating dermatologic patients.

W th few exceptions, some radiat on reached the gonadal areas of most patients treated by conventional dermatologic x-ray equipment and technics Some of the findings could ha e been assumed and anticipated, especially the doses obtained when irradiating dermatoses near the gonads or when the x-ray tube was d rected toward the gonadal areas. How ever the fact that radiation reached the gonads despite ex tensi e local shield ng relatively large tube-to-gonad di tances and angling th tube away from the gonad was not xpected.

The total amount of radiation that might reach the gonads f patient during s ngle dermatologic treatment (or n a complete series f treatments) may be higher or lower than the ggreated allowable l m ts (to the population as a whole) of 0 15 (150 m)/year depending on the conditions under which radiation is given. The dose howe er s less than the allowable maximum of 0.3 r (300 mr)/week for 13 week or a a erage f 0 1 r (100 mr)/week throughout the year establ shed for the mall segment of population occupationally exposed Under exceptional circumstances, despite precautionary measures, th gonad dose may well e ceed either allowabl dose

The a thor find ngs point up the need for a critical re iew a d evaluation f indications fo and benefits of x ray diagnosis and therapy as well a the need fo dev lopment d use of impro ed techn cs and equ pment to reduc x radiation eaching the gonads A joint responsib lity for finding ways to reduce the amount of x-radiation rea hing the gonads during med cal x irradiation must be shared by designers and manufacturer of x ray equipment, by radia i n phys cists and by physicians and radiation techn cia s

Diagnosti and therapeuti units need redesigning to re duc to a min mum the amount of tray and scattered rad ation Physicists need to mea ur stray and scattered radi tion to be able to advise on method and mean for reducing the gonad dose. Physician and medical personnel u ing radiation hould ealize that during diagnosti and thera

below the accepted weekly permissible average dose of 100 mr

However the survey revealed that there was an undue amount of stray radiation when the x ray apparatus was in use. Stray radiation in the corridors was high There was no lead lining in the walls. The explanation for the low exposure of personnel according to the film badges is that the x ray apparatus was in operation only a few hours every week.

The importance of standing well behind the protecting shield of the control booth of the x ray apparatus was emphasized by a reading of 1 000 mr/hour at the entrance to the booth. While the x ray machine is running the operator standing at the site of maximum protection inside the control booth is exposed to a significant amount of radiation. At this site, the maximum permissible average dose of 100 mr/week *is reached in slightly over 8 hours.*

► [We hope that this article will alert all those who administer ionizing radiation in management of diseases of the skin to survey their quarters and make certain that the operators of their equipment are properly and adequately protected against exposure to such radiation It is our opinion that the physician responsible for the administration of such radiation should make known to the physicist entrusted with the calibration of his radiation equipment any questions that he might have concerning radiation protection The responsibility of the physicist today goes beyond measuring the output of the machines and supplying a written report he should also seek and measure any sources of radiation which might act as hazards to the operating personnel Such detailed surveys should be done at the time of the installation of the radiation equipment where this has not been done there is no time like the present.—Ed]

Studies on Quantity of Radiation Reaching Gonadal Areas during Dermatologic X ray Therapy.—II *Methods quantitative measurements and analysis of some important factors influencing gonad dose.*—Victor H Witten Marion B Sulzberger and William D Stewart[7] (New York Univ Post Grad. Med School and Skin and Cancer Unit) attempted to evaluate the effects of a large variety of factors which could influence the gonad dose of x radiation The most important factors are (1) distance from the x ray tube to the gonads (2) tilt of the tube in relation to the gonad (3) position of the patient, (4) scattered radiation from various sources and (5) leakage radiation from the tubehead

In an attempt to reduce the number of variables present in

(7) A.M.A. Arch Dermat 76:683-693 December 1957

A lead cone devised to extend from the x ray tube aperture to the surf ce being irradiated nd to border the field to be irradiated reduced the gonad dose in the seated phantom by 50% The cone decreased the gonad dose by el minating the peripheral or outer portions of the primary x ray beam These portions of the primary beam appear to produce most of the scatter from the table and to be the source of direct radiation to the gonads of patients seated lose to the table. Reduction of the si e of the irradiated field, direct shielding of the gonad area and use of a sandbag for supporting the treated part pro ed effective in reducing the gonad dose. A combination of these technics can reduce this dose 97%

Th technics recommended for reducing the gonad dose are all readily available, inexpensi e, relatively speedy and simpl cause no discomfort or undue alarm to the patient and re effective in reducing the dose to a level such that the concern now oiced o er the possible genetic effects of ther apeutic radiation at least as given for most dermatologic disorders, may be greatly alleviated.

► [Although there are no reports of genetic damage having actually been produced by properly administered dermatologic x-ray therapy all possible measures must be taken to reduce the gonad dose to the absolute minimum We hav utilized the inexpensiv and simple protecti technics described in this report with no difficulty Patients occasionally ask what we are rapping around their midriff and why W tell them frankly that it is sheet of leaded rubber intended to offer them every protection possible and they seem to accept this explanation without larm —Eds.]

Clinical Evaluation of Radiation Therapy in Psoriasis. Leonard C Harber* (Rigshosp Copenhagen) compared the effecti enes f co entional x ray and grenz rays in treat ment f 76 unselected patients with psoriasis. X rays were dministered in doses of 160 r once a week using 50 kv 40 ma and 1 mm Al w th half value layer of 0.85 mm. Al. G en ray were gi en n doses of 200 r once a week, us ng 11 k 15 ma half alue layer 0.022 mm Al and 12 cm. d s tan In each case large pat hes of psoria s were divided to three areas one wa treated with x rays another with gren ray and the thir l w u treated and used a a co trol If larg pat hes were not available, three small, discrete pat hes were used.

A marked differenc was observed n the impro ement of irradiated sites compared with non irradiated controls. Im-

* A M Arch. Dermat. 77 334 338, May 958

peutic procedures they and their patients may receive x radiation to the gonadal areas Thus every effort should be made to reduce gonad doses to the lowest level consistent with effective use The physician must know the various sources of radiation reaching the gonads and master technics to reduce or eliminate the gonad dose

III Shielding technics and other precautions for reducing gonad dose—Stewart Witten and Sulzberger[8] investigated these technics on the basis of measurements made of the amount of ionizing radiation reaching the "gonadal areas of a pressed wood phantom Previous studies showed that the dosimeter readings recorded in the phantom corresponded closely with those recorded by dosimeters placed on the skin as close as feasible to the gonadal area of patients receiving as nearly as possible similar amounts of radiation under similar conditions Measurements were made with Keleket K 112 pocket dosimeters with a recording range of 0-200 mr

A lead rubber sheet, 1/16 in thick, wrapped around the lower two thirds of the phantom lying horizontally on the x ray table reduced the gonad dose from therapeutic radiation to the upper chest or back by about 50% This indicates that about half the radiation reaching the gonad area of the phantom under shielded conditions apparently is from leakage and external scatter radiation and the other half is in part scatter from the primary beam originating within the phantom itself The gonad dose can be further reduced by using therapeutic radiation of lower kilovoltage Reducing the kilovoltage from 90 to 52 reduced the gonad dose to an average of 20% of the dose recorded in the unshielded phantom irradiated with the higher kilovoltage

The phantom studies imply that when patients are treated in a seated position in a chair adjacent to the x ray table the ovarian area in females may be expected to receive less than half the amount of radiation which will be received by the male gonads Approximately three fourths of the gonad dose in a seated patient originates as scatter from the table and adjacent structures The remaining one fourth comes directly through the x ray tube head as leakage and from the peripheral portion of the primary beam

(8) J Invest. Dermat 30 237 247 May 1958.

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A marked difference was observed in the mpro ement of irradiated sites compared with nonirradiated controls. Im

* M A. Arch. Derm. 77:314 318, Mar 58

provement was less marked in large patches with large flaking scale and lichenification than in large patches with micaceous scale and less prominent lichenification or small discrete patches. In over 70% of the studies there was no significant difference in the degrees of improvement produced by the two types of irradiation. Improvement was discernible in about 50% of cases after only one treatment but the greatest improvement in irradiated sites occurred after two or three weekly treatments.

When improvement occurred in the control it was uniform throughout the entire area; the portion of the control nearest the irradiated site did not improve more than the central area. This fact plus the striking difference in improvement noted between irradiated and nonirradiated areas strongly reinforces the concept that irradiation produces improvement through direct cellular action rather than by release of a humoral substance.

► [This study once more confirms that grenz rays (half value layer 0.022 mm. Al) are as effective as x rays (half value layer 0.85 mm. Al) in causing involution of psoriatic patches. It does not provide data on the duration of the improvement. In our clinical experience the beneficial effect of x-rays is longer lasting in psoriasis than that of grenz rays. However, this difference in effectiveness is amply compensated for by the fact that grenz ray treatments to individual areas can be repeated with infinitely greater safety than x ray treatment; thus the patient can derive the benefits of repeated courses of grenz ray therapy over the years.—Eds.]

Investigations on Optimal Dosage in Treatment of Skin Carcinoma are reported by M. K. [illegible] [1] (The Hague). Introduction of reliable dosimeters and x ray tubes with beryllium windows has made it possible to develop technics of irradiation of skin malignancies which limit the dosage largely to the diseased tissue. Penetration of x ray energy beyond the skin tumor was limited by Flaats by bringing the focus as near as possible to the skin and by using radiation generated at 50 kv. by a tube with a window with a filter equivalent of 0.2 mm. Al. His method proved excellent for treatment of skin carcinomas except for the obvious drawback that because of the short skin focus distance the field that can be exposed to a homogeneous surface dose has only a small diameter.

The author found that by using 25 kv., 0.2 mm. Al filter (half value layer 0.1 mm. Al) and a focus skin distance of

(1) J. belge radiol. 41: 37-58, 1958.

10 cm., he could obtain a depth dose almost identical with that of the Plaats apparatu used at 2 cm focus-skin distance. By using the same kilo oltage without filter and a half value layer 0.043 mm. Al an e en greater percentage of the radiation energy could be confined to the first few millimeters of tissue. The chief advantages of this technic are the enhanced safety factor and excellent cosmetic results.

By measurement of the depth of skin carcinomas and precancerous lesions in 207 biopsy specimens, most skin cancers, senile keratoses and lesions of Bowen's disease were found to be less than 3 mm. thick. About one third of the carcinomas and all the precancerous lesions were less than 2 mm thick. In treating uch lesions, the dose should be adjusted as accurately as possible to the actual thickness of malignant tissue.

The author treated 102 cutaneous carcinomas, using a depth dose of 3,000 r In the original article a table is given showing surface doses which may be used to obtain 3,000 r at various depths. To avoid unnecessary complications in most cases 25 kv unfiltered, was used f r irradiation up to 3 mm. depth, and 25 kv with 0.2 mm Al filter for deeper irradiation. Usually the total dose was given in 1 session. The dose was fractionated only in tumors more than 3 mm thick, of great diameter or lying just over bone or cartilage

After such treatment there were primary recurrences in 8 of the 102 carcinomas. A 5-year primary cure rate of 78% was obtained. This rate actually gives an unfa orable impression of the results because with this method of treatment recurrences are easily re-treated without danger of sequelae. In the present group all ecurrences except 2 in which surgery was ind cated were re-irradiated and the patients have remained ymptom free. The recurrences originated in the margi f the irradiated field and apparently were due to irradiation f too narrow a margin of apparently healthy ti ue around the tumor o to multicentric origin of the tumor All lesions that recurred were basal cell carcinomas.

► [In this study an attempt is made to correlate the quality of radiation used ith the histologically established approximate thickness of the lesions. This is in keeping ith the principle that quality and dose of radiation should be selected so as to destroy the skin cancer without extensive damage to the surrounding and underlying structures. The question whether the high rate of failures as actually due to the reasons given by the author remains unanswered.

We are staunch advocates of applying the principle of using a selected quality and dose of radiation in the management of benign skin lesions also. In this way the undesirable effects of irradiation can be avoided and safety" will become a word with meaning.—Eds.]

Treatment of Carcinoma of Alae Nasi by Fractional Doses of X rays is advocated by Norman M Wrong[2] (Univ of Toronto) because this method produces a good cosmetic result with a minimum of undesirable sequelae and a low recurrence rate.

METHOD.—*A total dose of 3,500–4,200 r was given, depending on* the size of the lesion. This was divided into 6 or 8 equal doses given daily At the first visit a biopsy specimen was taken, and if necessary the growth was flattened to skin level by electrodesiccation. A small plug of gauze impregnated with zinc ointment was inserted into the nostril to protect the septum when the roentgen treatments were given.

The quality of radiation used in treatment of basal cell carcinoma of the alae nasi is important, and the softer the x ray used the better the effect, as most of the rays would be absorbed in the ala. In the *present series factors were 70 kv., 5 ma target skin distance 4½ in.,* no added filter half value layer 0.77 mm. Al

The alae nasi appear to be particularly prone to basal cell carcinoma *Of 112 consecutive skin malignancies 27 in*volved the alae nasi and all were basal cell carcinomas. None of the *27* lesions recurred after treatment with fractional doses of x ray Follow up has been 6 months to 5 years. Larger lesions have been replaced by white depigmented scars but none has shown any pronounced telangiectasia. In no case has there been persistent soreness of the nose after treatment.

► [The methods and total dosages described by the author are similar to those used by many dermatologists in the United States and Canada. They generally produce excellent therapeutic and cosmetic results. Of course there is a lower limit to the softness of the radiation which may be used We usually administer treatment at intervals of 2 days rather than daily although the total dose (ordinarily greater than 4000 r) is given in essentially the same period of time.—Ed.]

Treatment of Myxomatous Cutaneous Cysts (synovial lesions of the skin) is discussed by *Robert B Engle[3] (Univ of* Southern California) The cause of these cysts is believed to be a focal degeneration of the corium Whether this results from local trauma, a small arterial thrombosis or some other factor is not known The first change is a degeneration or resorption of the collagen in a localized area leaving fibro

(2) A.M.A. Arch. Dermat. 77:73-78, January 1958.
(3) Radiology 71:93-95, July 1958.

blasts with but little intercellular material. Basophilic mu coid material collects between the fibroblasts and they gradually disintegrate, creating multiple minute cavities which coalesce to form a gross cyst containing clear glairy gelat inous or syrupy fluid. This fluid is not secretory but arises from degeneration of local connective tissue. The inner wall of the cyst is irregular at first. Later it becomes smoother and denser There is no epithelial or endothelial lining No communication exists with subjacent structures such as ten dons, joints or bursae.

Myxomatous cutaneous cysts treated by incision and drainage, curettage cauterization, fulguration free ing with carbo dio ide snow and surgical excision invariably recur In general radiation therapy is indicated. The author de scribes 4 patients treated with x rays. Two cysts failed to respond to doses of 1 000 r superficial x-irradiation (100 kv 3 2 mm. Al 25 cm target-skin distance. One cyst showed a partial esponse (satisfactory to the patient) to a single dose of 2,000 r The fourth cyst responded to 1 400 r of more penetrating radiation (half alue layer 1.2 mm. Cu) Further tud es of the optimal qual ty and quantity of radiation for these lesions are indicated.

► [W have had satisfactory results with *fractional* x-ray therapy of some myxomal" cyst However seemingly more logical form of treatment, that of injecting hyaluronidase, was suggested by Götz and Koch (Arch klin u exper Dermat 204 361, 1957) —Eds]

Results of Chaoul s Method of X ray Treatment (Contact Therapy) in Skin Cancer Branislav Gadjanski[4] (Univ of Belgrade) reports on the 3-year results in 450 patients who had x ray contact therapy for skin cancer In all but 25 the cance was localized in the face. There was no sex predilec tion B sal and prickle cell cancers had about the same incidence Papillomas, especially those of the lip were considered maligna t tumors some metastasized later

Of 339 patients available for the first follow-up examina tion, about 1 3 month after treatment completion 74% were mptom free After 3 years, 41.5% were asymptomatic, 1 3% were impro ed and in 3.5% treatment failed. The death rate was 6% but only 1.35% d ed of their skin condition. No follow-up studies were available in 47.5% of the patients. Necrosis was encountered mostly in elderly thin patients,

) Radiol [illegible] 5 [illegible], 1957

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th usefulness to hemangiomas that are not o er 2 3 mm thick.

I the first treatment series total dose of 3,000 rep was given, d vided into single doses of 1,000 rep each 1 week part After 6 weeks the lesion wa re-evaluated. If suffi cient egression had not occurred, another 1,000 rep was del ered. Follow-up examination were one e ery 6 weeks and, when necessary 1 000 rep was repeated each time until e -all dose of 6,000 rep was reached.

After the second o third sitting the hemangiomas usually hanged from bluish red to a lighter red and its urface be- me smooth. If healthy skin was ncluded n the radiation ea, some erythema appeared there About 6 weeks after the first treatment series previ usly elevated hemangiomas had regressed to skin level. Occasionally a pigmented area ap- peared around the radiation site.

[Sr90 is good source for pure beta radiation When prepared in the form of ell-constructed plaques, it is safe to use as surface applicator Great care must be taken however to make certain that ther are no leaks from the irradiating source since Sr90 localizes in bone and is dangerous compound hen absorbed in the mouth or other routes —Eds]

Hemangiomas Treated and Untreated. George C. Andrew Anthony V Domonkos, V cto M Torres-Rodriguez and John K. Bembenista (Columbia Uni Presbyterian Med Center) studied th records of 1 113 patients (710 fe mal) w th ascula nevi Of these 329 had hemangioma impl (trawberry mark) a d 584 had hemangioma caver nos m Of 153 pat ent w th hema gioma simplex who re ei ed no treatment 102 were observed adequately In 64 (63) the lesion i luted or mproved within 5 years wherea 38 (37%) the hemangiomas persisted. In patients who had hemangioma implex with spontaneous involution, 83 f th lesion wer 1 cm or les m diameter It may be ncl ded that an hemangioma implex on the f e measur g 1 cm or more hould be treated with out delay because those f larger iz ha poor pos b lities of n olution without therapy Occa ionally a large hemangioma disap- pea pontaneou l without scar but other have been noted t per t, grow ulcerate and bec me a serious problem. Be- se th cosmetic ppearance of the sit is usually the most mportant con deration ea ly in titution of treatment and

especially when the skin in the treatment area was atrophic or tightly stretched over the underlying bone such as on the ridge of the nose over the zygoma or in the corner of the eye.

The author did not use very large radiation fields because *the peripheral areas of large lesions do not get enough radia tion if one field is used* This may lead to peripheral recur rences

TECHNIC.—The Siemens-Monopan machine was used and almost always an oblique electrode was applied. Average total dose was 6 000 r divided into daily doses of 500-600 r To prevent necroses, fixed fields were avoided and moving fields were used. Radiation was given until the lesion eroded, causing the tumor to melt away Grat ifying cosmetic results were achieved by covering the treatment area with a thin sheet of cellophane, which prevented development of brown pigment rings around the smooth scar

Chaoul s treatment method should not be applied to pa tients who previously had x ray ra lium surgical or coagu lation therapy because these methods lead to unphysiologic conditions in the stroma with subsequent severe circulatory disturbances that hinder reparative processes

***Strontium-90 Dermaplates and Their Use in Treatment* of Hemangiomas** were studied by R Gersing[5] (Bonn Ger many) Among the beta radiating isotopes suitable for su perficial treatment Sr^{90} is especially favored because it has a long half life (25 years) and is available in ufficient amounts Sr^{90} decays into Yt^{90} which has a half life of 61 hours and transforms into stable Zr^{90} Sr^{90} and its decay products are pure beta emitters In closed carriers as used in therapeutic applicators the two isotope are in radioactive equilibrium The dermaplates are cylinders made of nickel the hollow part of which contains the radioactive substance The window of the cylinder is 0 1 mm thick and permeable to beta radiation whereas the top i 1 5 mm thick and im permeable to radiation The diameter of the commercially available cylinders is 9 9 16.5 or 23 mm The two derma plates used by the author had radiation activity of 20 mc /4 sq cm. and 100 mc /2 sq cm respectively

The limited penetration of Sr^{90} make it p ible to treat hemangiomas over radiation sensitive area uch as growth zones of bones near the breast glands and over the eyes (lid hemangiomas) The steep decline of the isod e curve limit

(5) Fortsch Geb Röntgenstrahlen 84:233 241 Februar 19 ?

not have recovered completely from the damage resulting from the first series of treatments. If a third or fourth course of treatment is given, symptoms of overexposure may appear When radiations with a half value layer of 2 mm. Al or more are used, the danger point is reached even sooner

When electrons from high-voltage generators are used for irradiation, the total body dose is considerably below that produced by x-rays. With 2.5 Mev electrons for application of 300 r to the skin, the average dose to the body is 67 r with 1 5 Mev electrons, the average total body dose is 36 r With electrons, therefore, it should be possible to treat cutaneous lesions with a higher dose and to treat recurrences more often with fewer symptoms of radiation damage to the body

In the treatment of extensive dermatoses, if monoenergetic electrons cannot be used, it is advisable to use x rays with a half value layer between 0.5 and 1 mm. Al An effort should be made to shield any part of the skin not involved to reduce the total dose delivered to the body

► *(This article points out one of the very important aspects to be considered when using ionizing radiation in the treatment of diseases of the skin Furthermore, it clearly demonstrates that here too it is advisable to use the softest effective radiation feasible in treating benign dermatoses. —Eds)*

Telepanirradiation of Generalized Dermatoses with Beryllium Window Tubes Dose Rate in Depth, Uniformity of Field and Illumination. Gian Luca Sannazzari and Giuseppe Lovera* (Univ of Turin) report that the introduction of apparatus with beryllium window tubes has created new and better techn cal possibil ties in dermatologic x radiation because t is now possible to deliver rays at a wa elength greate than e e before (those generated by energy of 15-50 kv) With these tubes at standard focus-skin distances (20-30 cm) the field of radiation ca be large the rays reaching the body are practically entirely bsorbed within the skin and th d ration f each s ttı g is brief With a filter variations half value layer can be obtained, making possible a true taneous stratitherapy

The energy filter combinations, preset n four witches w t h 1 10 k w thout filter sw tch 2, 29 kv 0.3 mm. Al witch 3 43 kv 0 6 mm. Al and switch 4 50 kv 1 mm. Al

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*Dermatologica 1 49 452 December 19 ?

prevention of secondary infection are recommended. The likelihood of ulceration of hemangiomas on the lips, nostrils, eyelids and ears suggests that these lesions should be treated even though they are less than 1 cm in diameter

Of 135 patients with hemangioma cavernosum who received no treatment during the first 5 years of life and who could be followed adequately 22 (16%) showed involution or improvement of the lesions during the 5 years. The high percentage of persistence in untreated cavernous hemangiomas indicates the desirability of treatment for all cavernous hemangiomas

The method of treatment should be carefully chosen to secure the best cosmetic results The authors feel that radium therapy properly administered assures excellent results without risk of radiation sequelae In some patients, surgical excision ligation solid carbon dioxide or roentgen ray treatment is indicated.

► [Some other authors have reported a much higher incidence of spontaneous cures. Regardless of the particular school of thought with which one agrees, it is the responsibility of the physician to advise the patient or his family whether therapy is required and if so to select the method of therapy best suited for managing the particular lesion. In instances in which treatment is considered unnecessary it is best to see the lesion at appropriate intervals in order to follow its course and institute active therapy if necessary.—Eds.]

Superficial Radiation Therapy of Large Skin Areas. R. Braams[7] (State Univ of Utrecht) calls attention to the relatively large doses of x rays that are delivered to the total body when extensive skin lesions are treated Experiments on monkeys have shown that a total body dose of 450-500 r x radiation delivered in a relatively short time (a few weeks) has a 50% chance of causing a lethal effect A total body dose of 450 r means that in the course of irradiation each part of the body received about 450 r The human 50% lethal dose is believed to be about the same as that for monkeys.

Braams presents a method for calculating the approximate total body dose after extensive irradiation of the skin surface. An average dose of 225-250 r is given to the whole body when the average patient receives 300 r (3 doses of 100 r each) with a half value layer of 1 mm Al to the total skin surface If such treatment is repeated in a year or less because of recurrence of the dermatosis it is probable that the body will

(7) Dermatologica 117:204-214, October 1958.

by soft x-rays, it i possible to deliver supersoft x rays. These new tubes thus allow irradiation only of the most su perfical layers of the kin (epidermis and papillary bod es) or of deeper laye s, as the need may arise

Brown reviewed statistically the therapeutic results in 773 patient treated fo eczema with x rays. Considerably better results were obtained with lower doses (60 r) and weak radi ation (tube with beryllium wi dow 30 kv 0 5 mm. Al and tubes with 0.3 mm. gla walls, 70 kv without filter) than w th higher doses (100 r) and stronger radiation (tube with glass wall, 100 kv 1 2 mm. Al)

E en n acute ec ema, in which x-ray treatment was for merly thought inadvisable good results were achieved by educing the dose to 10-15 r

[We also are in favor of carefully selecting the particular quality of radiation best suited to treat the particular skin disease with the thought of delivering the radiation as much as possible within the invol ed portions of the skin As most benign dermatoses are limited within the uppermost 1 mm of tissue, it is logical to use radiation softer than that conventionally applied in dermatologic therapy (half-value layer of 0 8-1 0 mm Al Grenz radiation with half-value layer of 0 018-0 036 mm Al is ideally suited for treatment of many of these dermatoses At times somewhat harder radiation with half value layer of 0 5 mm Al may be used Knowl edge of the depth-dose curv for the arious qualities of radiation w ll be of distinct help in deciding on the most suitable type of radiation to use Ed.)

Radiation Damage Caused by Shoe-Fitting Fluoroscope

H Kopp (Finsen In t., Copenhagen) report a case

Woman, 56, had typical radiodermatitis of the dorsal surface of the right toes with cicatricial changes, her toes scaling, depigmentation, telangiectasia and ulceration. She allegedly had never had radi ation treatment or ray examinations. She had, however worked for 10 years in shoe hop where tw shoe-fitting fluoroscopes were used

Examination of the machines revealed that in one the beam intensity at the foot plate w 9.. / minute and in the other 13.. minute A defecti lead screen in one fluoroscope exposed the shop assistant to strong diffuse radiation while she operated the machine From the front part of the foot plate an unscreened cone of ray passed in the direction of the customer abdomen, delivering 1 / min in adult and considerably more in children.

The patient radiodermatitis had apparently resulted from ex posure of the foot while demonstrating the fluoroscope to apprehen children, while trying new shoe model under transillumination and while supporting the right foot on the platform in front of the foot opening while examining customers feet.

Brit M J 344 14 Dec 7 957

Some values were measured with the phantom chamber for soft rays and Siemens universal dosimeter The rate of distribution in depth along the central ray was at a distance of 1 m half the dose with switches 2 3 and 4 at 5 5 12 and 18 mm respectively and at a distance of 2 m half the dose with the switches at 7 5 17 and 26 5 mm The depth at which 70% of the dose was delivered along a line perpendicular to the axis of the tube while moving away from the center of the field was at a distance of 1 m with switches 2 3 and 4 39 44 and 48 cm from the center and at a distance of 2 m 53 77 and 87 cm from the center The intensity of radiation at a distance of 1 m with switches 2 3 and 4 was 7 5 9.7 and 9 1 r/minute and at a distance of 2 m 1 5 2.6 and 2.5 r/minute.

These results indicate that beryllium window tubes are valuable tools for total body irradiation at a distance for generalized dermatoses

► [After the article by Schirren (J Invest. Dermat 24 463, 1955) on teleroentgen therapy with soft radiation from beryllium window tubes, a special x ray unit installed by the Picker X ray Company has been used for similar therapy at the New York Skin and Cancer Unit It operates at 50 kv., 25 ma., with a half value layer of 0 2 mm. Al at a distance of 2 m. In our limited experience with this modality it has proved beneficial in some cases of widespread eruption —Eds.]

Comparative Statistical Studies on Influence of Hardness of Radiation and Size of Dose on Results of X ray Treatment of Eczema were conducted by Roy Hershel Brown[9] (Univ Skin Clinic, Zurich) There has been growing tendency to economize with the therapeutic effects of x rays. In treatments in which cumulative effects have to be expected exceeding the dose needed for therapeutic effects is a mistake This is true especially for treatment of inflammatory changes as opposed to treatment of neoplasm In the latter possible severe tissue damage can be overlooked for the sake of cure but in the former even relatively slight damage may be considered a failure Because inflammatory diseases involve only a few millimeters of superficial skin tissues it is senseless to apply rays that penetrate many centimeters into the body and exert superfluous or even harmful effects

Superficial x ray treatment has become possible by recently developed x ray tubes that operate on 6-50 or 6-100 kv Due to a beryllium window which can be easily penetrated

(9) Dermatologica 117:215-223, October 1958.

m mbranes, and co sists of irregular slowly expanding spots of gray-brown to blue-black. Coloration is uneven. Tu morous transformation usually takes place late, at one or several sites. Recognition of these spots is important because they regress well under x ray therapy A third group of mel anomas develops spontaneously on previously normal skin. Melanomas are usually dark blush black. Occasionally they may be poor in pigment or even unpigmented. These may lead to serious m sdiagnoses, especially when pigment is completely absent (amelanotic melanoma)

Early recognition of a melanoma is important. If diagnosis is do btful, t should not be confirmed by biopsy because of pos ible traumatic spread. Rather the tumor should be treated as i its mal gnancy were proved. The lesion hould be destroyed by coagulation or excision, far into the healthy area. Lately the authors have administered x radiation once, about 3,000 r followed mmediately by excision. Even when the regional lymph nodes appear uninvolved p ognosis will be improved by their removal Irradiation of involved lymph nodes is advisabl before their removal. If there are cutane- and bcutaneous metastases around the tumor only a ery wide, deep excision (including the fascia) may be suc es ful If the tumor and the metastases involve an extremity amputation may be necessary Metastases to internal organs lenot e tremely poor prognosis.

The autho reviewed therapeutic results after 5 years in 104 m l noma At tim of treatment, 70 of these had no me ta ta es (tage I) 30 showed regional metastases (stage II) whereas 4 had metastases to nternal organs (stage III) Aft er 5 ears 61% of the patients in stage I were free from mptom 11 5% n stage II and none in stage III Best results w ch eved with melanomas of the head Primary melanomas were not resistant to radiation treatment.

W th competent treatment neither the urgical no the ay method can be sa d to be superior

[In previous years, Miescher continues to advocate the use of x-radiation as part of the management of malignant melanomas. As pointed out in this article, he actually feels that -ray therapy is equal to surgical therapy provided it is done in competent manner —Eds]

Malignant Melanoma Combined Surgical and Radiotherapeutic Approach. Robert J Dickson[3] (Johns Hopkins

[3] Am. J Roentgenol 79 1043-1070, June, 1958

Besides the hazard of radiodermatitis from use of shoe-fitting fluoroscopes the author calls attention to the hazard of increased gonad radiation The dose of radiation to the customer's abdomen during a typical foot examination with the machine [illegible] greater than that from [illegible] the genetic hazards, [illegible] be considered. This adds to the difference, because shoe fitting fluoroscopes are used chiefly for child customers whereas x ray examinations are made more frequently in older persons.

► [It is unbelievable that the use of shoe-fitting fluoroscopes still is permitted in some states and countries. As indicated in Kopp's study there was not only radiation exposure of the customer's feet but also of the gonadal and other areas, not to speak of the exposures received by the sales personnel routinely using the machines.—Eds]

Treatment of Melanomas is described by G Miescher and A Hunziker[2] (Univ Skin Clinic Zurich) Successful treatment of malignant tumors depends on early recognition This criterion is generally not difficult to fulfil in skin tumors and thus the cure rates become practically 100% in basal cell and prickle cell epitheliomas of small or moderate size Malignant melanomas however are an exception They have a strong tendency to metastasize due to their characteristic cells which grow by infiltration and also due to their close relation to the lymph vessels and blood vessels The tumors spread through the lymphatics and through the blood stream. Metastases may appear very early while the tumor is only of pinhead size and involve all organs or only after 10-20 years which would indicate that melanoma cells may remain dormant in various tissues

Melanomas often start from a pigmented nevus There seem to be no nevus types predisposing to malignancy Characteristics that point to malignant transformation of a nevus are sudden increase in growth usually accompanied by increasing pigmentation signs of inflammation bleeding or crust formation and itching Darkening of the nevus without increase in size and without inflammation does not indicate malignancy

Malignant melanomas may develop from melanotic precancerous areas This form of precancerous state is common est in the face and on the hands occasionally on the mucous

(2) Schweiz. med. Wchnschr 84:203-205, 31 1 1954

was no statistical difference between results of local therapy and those of wide surgical excision, but the groups were fairly small. In a comparison of patients treated surgically and those in whom radiation therapy was used there was considerable improvement with the addition of radiation therapy. However the difference in survival rates was just statistically significant, and these figures cannot be advanced as definite proof of the advantage of giving radiation therapy to these patients. On the other hand, the patients in the different groups were probably not strictly comparable. First, the patients treated by surgery alone were probably in a relatively earlier stage of the disease. Second, many patients with more-advanced cases were treated by irradiation and were included in that group. These considerations lend force to the suggestion that postoperative and palliative radiation therapy tends to improve the prognosis in malignant melanoma.

The natural history of malignant melanoma is variable, and even in apparently advanced cases long term survival is frequent. The present series may include a high proportion of such cases or there may have been a relatively large number of patients with early stages of the disease. Attempts were made therefore to compare this series with others from the literature in regard to age, sex, body distribution and staging, and it would appear that there is a fair degree of similarity. The 5-year results of wide surgical excision alone were comparable with others reported in the literature but when radiation therapy in adequate dosage was given a higher survival rate was obtained. When the material is broken down into stages, the number of patients who survived more than 5 years in stages I and II is increased (stage I 50%, stage II 23.6%). Prognosis in stage III is still negligible.

Though the evaluation of any treatment method is difficult in such an unpredictable disease, the improvement in survival rate over that reported by other authors totaling nearly 2,500 cases, indicates a substantially beneficial effect from postoperative and palliative radiation therapy. The opinion that radiation therapy is valueless in malignant melanoma is probably based on experience with inadequate dosage.

► It is gratifying to see that the management of melanoma is being re-

Hosp) describes results of treatment of 234 patients with malignant melanoma seen at Toronto General Hospital, Johns Hopkins Hospital and the USPHS Hospital Baltimore There were 102 patients (43.5%) in stage I (localized melanoma confined to skin including local recurrences and nearby deposits in cutaneous lymphatics) 93 patients (39.3%) in stage II (with regional lymph node metastases confined to one node station only) and 39 patients (16.7%) in stage III (with metastatic involvement of two or more groups of nodes or distant metastases)

The treatment policy at Toronto General Hospital was to operate on all patients in stages I II and occasionally III with wide excision of the primary tumor and the immediate lymph drainage areas and then to give postoperative radiation therapy to all areas found on histologic examination to contain disease Not infrequently however only surgery was used A few patients at the two Baltimore hospitals were treated by surgery with irradiation but most received no radiation therapy except as palliative treatment of recurrences.

Radium and roentgen rays were used with almost equal frequency Teleradium therapy both to primary and metastatic sites was given to several patients the dosage varying between 4,800 and 6 500 r in 4-6 weeks Those receiving roentgen therapy were usually given 100 kv radiation to a dose of 5 000 r in 10 days to the primary area with an estimated tumor dose of 4 000-5 000 r to lymph node bearing areas at either 200 or 400 kv in about 5 weeks

In 71 patients initial treatment consisted in application of caustic solutions or local surgical removal without any further treatment within a 1 month period 42 were treated by definitive surgery and the other 121 received radiation therapy immediately after the initial surgical intervention In many patients the surgery was local and many stage III patients were included in the group receiving radiation therapy

Of the 121 patients in whom radiation therapy was used 41% survived 5 years. About one fourth of those treated by excisional surgery without irradiation lived 5 years and about one fifth of those having only local therapy during the 1st month of treatment were still alive for this period There

t 3 minutes and Mexicans or Sicilians at 5 minutes. Subsequent exposures as tolerance develops rarely exceed 12 minutes except for Mexicans. Several thousand treatments have been given in the ultraviolet cabinet and patient acceptance has been excellent. Pityriasis rosea, psoriasis, atopic eczema, neurodermatitis and other generalized dermatoses have continued to respond at least as well as to cold or hot quartz therapy

The ultraviolet cabinet has several advantages. Irradiation of the entire body requires about one fifth of the time needed with other technics. No warm up period is necessary fo the lamps and no cooling-off period is requ red before euse Heat production is minimal the lamps can be touched t any tim without discomfort. Because the tubes are lateral to the patient, there is no chance of spontaneous or induced breakage leaki g hot mercury by gravity on a patient below th light source with resultant thermal burn. Ultraviolet co erage of the entire skin surface is more uniform than with standard technics. Installation, operation and maintenance are easy and economical

The only untoward incident in 4 years operation occurred when patient who had many exposures prev ously removed the goggles nd read by the light of the 8 lamps for a 12 minute exposure. A mild keratoconjunctivitis resulted.

D Surgical Therapy

Indications for Abrasive Therapy are described by E. H Hermans S and E. H Hermans Jr[3] (Rotterdam) Generally any skin abnormality that is due to a disease congenital malf rmation o accident can be considered for abrasive therapy independently of its size Abrasi e therapy should not be tri d on persons who have a tendency to extensive keloid formations or in skin diseases that are not yet quiescent Th more disturb ng the cosmetic changes, the better will be the results of abras ve therapy

I dications for abras ve therapy are grouped according to the degree of difficulty n olved n handling them (1) lesion which protrude from th skin such as fibromatous or verrucoid nevi, hyperkeratoses hinophyma, etc.—the least

(3) Hautarzt 37 376, August, 1956.

evaluated and revised. There is much evidence that malignant melanomas are not as radioresistant as some of the vociferous advocates of exclusive use of surgery (and sometimes *of extremely radical surgery at that*) would have us believe.

Miescher (A.M.A. Arch. Dermat. 200:215, 1955) pointed out years ago that the supposed radioresistance of malignant melanoma should not prevent one from using radiation therapy for these lesions (see also preceding article). Jørgsholm and Engdahl (Acta radiol. 44:417, 1955) reported surprisingly good results from radiotherapy alone. Evidence such as this is accumulating and we sincerely hope that the *near future will bring* cooperative efforts between dermatologists, surgeons and radiologists in the attempt to improve the favorable results in the management of this frequently fatal tumor.—Eds.]

Ultraviolet Light Therapy: Utilization of Tubular Fluorescent Lamps in Cabinet for Generalized Simultaneous Irradiation is described by Murray C. Zimmerman[4] (Univ. of Southern California). The ultraviolet source is 8 Westinghouse fluorescent sun lamps 48 in. long 40 watt FS40T12. *Two of these lamps fit into each of four standard bipin double socket 48-in. fluorescent fixtures*. The cabinet is 3½×2½ ft. set in a 5½×6 ft. dressing room. A fluorescent fixture with 2 lamps is set vertically at each corner. The tubes are turned on by a 15-minute automatic electric timer switch, similar to the x-ray timer. The patient is observed through an ultraviolet-opaque window. The surrounding dressing room is convenient but not necessary. The cabinet arrange*ment can be used in any closet bigger than 2 [illegible] ft. [illegible]uare or* in a 2½ ft. corner of the treatment room.

Technic.—The patient [illegible] escorted into the dressing room, told to disrobe completely except for shoes and socks, then to knock on the outside door for the nurse. As the nurse enters the dressing room, the patient steps into the ultraviolet cabinet and shuts the door. Skolex Sunscreen cream *is smeared thinly on the nipples of all patients* and on the glans of circumcised males. The patient wears protective goggles or, if there are no facial lesions, a towel *may be wrapped around* the head and held with the hands locked behind the neck. The nurse turns on the timer, then sets a second separate spring timer to ring a [illegible] *timer shuts off the lights*. The pa[illegible] [illegible] when the bell [illegible] or the [illegible] [illegible] at the patient stands in the [illegible] with the feet [illegible] apart. He stands still or alternate[illegible] [illegible] knees to expose the medial thighs, if these are involved.

The light source has a continuous ultraviolet spectrum 90% between 2,800 and 3,100 A. Thin skinned blondes or redheads are started at 1 minute *exposures*; *dark brunette*

(4) A.M.A. Arch. Dermat. 78:446-452, November 19[illegible]

thi method of treatment were skeptical about its usefulness for precancerous conditions.

Of 33 correspondents with experience in the use of derma brasion for actinic or senile skin, 30 were enthusiastic or satisfied with results obtained. Over 1,300 patients have been treated by this group. Protection is relative rather than absolute, since some new keratoses or epitheliomas develop in pla ed areas. However recurrences are much less frequent than n adjacent unplaned skin or before performance of the prophylactic procedure.

Some dermatologists have used planing to remove single keratoses Though this is a successful method Ringrose in unpublished work has shown that freezing with dichlorotetrafluoroethane (Freon 114) removes the keratoses as well does freezi g followed by planing If further investiga tion confirms this observation then dermabrasion is indicated in the treatment of premalignant skin only as a prophylactic measure, since simple freezing is much easier on the patient than plan ng

Chronic radiodermatitis was planed by 22 dermatologists, w th experience in 101 cases. Eleven who eported found the procedure satisfactory 3 fair and 8 poor or unsatisfactory Most of the criticism revolved around scarring and slow heal ing The author points out that chronic rad odermatiti is more than cosmetic defect, so results in thi condition should not be judged by the standards appl ed to treatment f acne scars Eradication of the tendency toward malignant degeneration is the aim of treatment. The time required for healing of no great importance Surgical excision and skin grafting are th onl other possible treatments in extens e ses f radiodermatitis. The morbidity and cost are much greater with uch procedu es than with plani g and the smetic result are often no better

F aluation f the t eatment of leukoplakia by planing is mi bl at thi tim because of lack of tensi e experi enc but the approach i feasibl prom ng a d nonscar n g Recurrences re the rule i xeroderma pigmentosum because the ba genetic weaknes is not emo ed Res lt m epithelioma adenoides cysticum ppear prom s g Good es lt in l patient w th arsenical keratoses were reported Some dermatologi ts reported excellent esult n the

difficult to treat (2) scars level with the skin surface such as after cut wounds operations plastic surgery etc (3) dimpled scars which can be treated satisfactorily if not too deep (4) deep scar such as in infiltrative forms of acne after herpes zoster smallpox etc. if not too large and atrophic (5) color changes in the skin surface due to rosacea, tattooing flat pigment nevi vascular nevi etc

Results of abrasive therapy besides depending on the type of skin changes depend also on the patient s age localization of the skin changes and the type of skin Thick skin with many appendages usually is more amenable to treatment than thin skin The older the patient the thinner and more atrophied is the skin and the poorer is its regenerative ability Very young persons also have extremely thin skin After puberty the skin is usually more suitable for treatment. The *extensor surface of the extremities* the back and the neck have a thicker skin than do the flexor surfaces or the abdomen The skin of the eyelids and at the angles of the mouth i extremely thin Persons with a dark complexion usually have thicker skin with more appendages than do fair skinned persons

► [In every patient, physical *and* psychologic finding (over-all attitude and acceptance of their acne and their acne scarring) must be considered before decision is made as t whether to carry out dermabra ion in acne scarring Furthermore the patient should be carefully instructed regarding the degree of improvement that can be anticipated All who have had experience with this technic certainly have encountered an occasional patient who is not sat fied with what has been accomplished regardless of how worth while and, mor frequently patient who are overenthusiastic about the esults achieved

In the abstracts that follow Epstein and Ayres *et al* advocate use of dermabrasion in actinic and senil ski show ng changes f trophy telangiectasia and keratoses a the best method of treatment for this particular precancerous *condition* —*Ed*]

Planing for Precancerous Skin Follow up Study i reported by Ervin Epstein[*] (Highland Alameda County Hosp. Oakland Calif) A questionnaire wa sent to 120 dermatologists known to use planing in their practice An swers from 103 indicated that there i relatively little di agreement among those with experience in the u e f derma brasion for precancerous skin Mo t feel that planing i a promising treatment especially for prevention of recur rences However many dermatologist who have not u ed

(6) A.M.A. Arch. Dermat. 77 676-681 June 1958

Pla ng provides a nonscarring method for treatment of keratoses, as well as a prophylaxis against skin cancer by replacing the sun-damaged, precancerous epidermis with n w epidermal cells derived from the cutaneous adnexa. Five depths f planing can be delineated during the planing pro- ed re (1) first the pigment vanishes indicating that the m portion of the basal cell layer has been removed (2) m riad f yellowish macules less than 0 5 mm in diameter nd cate that the upper derm s has been reached making th p losebaceous apparatus visible (3) as plani g goes deeper the urface ppears studded w th yellowish lobulated pap les, which ar the sebaceous glands that ha e been cut ros and is the depth usually achieved in moderately deep plan ng (4) if plan ng is carried deeper decided resistance f the tissues is encountered, primarily because the tissue is below the penetration of freezing (about 2 mm.) If freezing done gain at this level further depth can be achieved with relat e ease, but caution is n order (5) If planing is carried still deeper yellow nubbins, which are lobules of subcutaneous fat, are exposed. This level is well below the sebaceous glands and at the depth of the deepest hair pa pillae. Planing at this level s likely to esult in removing so much dnexa as to cause scar formation.

Results of experiments on the comparative effects of re frigera t on an mal and human skin ind cate that human facial kin can tolerate considerable freezing with ethyl chloride d hlorotetrafluoroethane (Freon 114) but that m xtures containing large proportions of the much colder l hl rod fluoromethane (Freon 12) may be undesirable. Refreezing an area of the skin to perform more adequate pla g not considered hazardous.

On f th uthors performed fi e full-face planings on 3 patient w th p tted acne scars who had typical keloids elsewher n the body In each, a small test area was first planed on the f c then, no untoward reaction having occurred in f weeks, the full face was planed All 3 patients had an en t rel sat factory course over ma y months after planing [I is encouraging to learn that patients ith acne scarring and keloids elsewhere on the body apparently may ha their face planed without formation of keloids at that area Of course, much additional experience in this regard is necessary —Eds]

treatment of superficial basal cell epithelioma by dermabrasion but others who have tried planing still prefer other methods of treatment The treatment of ordinary basal cell and squamous *cell* epitheliomas by planing needs further investigation It is certainly not the treatment of choice However it can be used safely in these lesions. Perhaps planing plus irradiation will eventually give the best cosmetic result and the highest percentage of cures in superficial neoplasms. It will never replace x irradiation mutilating surgery or chemosurgery for far-advanced growths. Possibly the most important finding is that planing does not spread skin cancers. Therefore it can be performed in the presence of epitheliomas.

► [Apparently planing is the best available form of treatment for actinic and senile skin even though sometimes senile keratoses may develop in the planed areas

To date there is no better method for the prophylactic care of precancerous skin Actually this could be a very important advance in dermatologic therapy and further experience with the method should be reported at intervals in the future

It is gratifying that no spreading occurred in the 32 cases of "ordinary" basal cell carcinoma treated by this method. However one may ask whether the evidence from this survey material is sufficient to rule out the possibility of seeding malignant cells during the planing procedure from which epitheliomas will grow at a later date —Eds]

Recent Developments in Surgical Skin Planing are described by Samuel Ayres III J Walter Wilson and Ralph Luikart, II[7] (Univ of Southern California) Steel wire brushes have been largely replaced by the less hazardous diamond or ruby chip burs or fraises and serrated steel wheels. The jet spray handpiece has been further improved. Drawing its refrigerant liquid continuously from a tank containing *more than needed even for prolonged operation* it eliminates the time necessary for the operator to change from a hand held can to the abrading tool thus increasing the convenience and *efficiency of the freezing planing procedure* The jet-spray handpiece has a spatter guard to protect the operator from the spray of abraded skin particles and blood similar device *are available to clip to the conventional* handpiece.

In addition to acne pits and wrinkling multiple a time (senile) keratoses are an important *indication for planing*

(7) California Med 88 127 132 February 1958.

Planing provides a nonscarring method for treatment of keratoses, as well as a prophylaxis against skin cancer by eplacing the sun-damaged precancerous epidermis with w epidermal cells derived from the cutaneous adnexa. F ve depths of planing can be delineated during the planing proced re (1) first the pigment van shes indicating that the majo portion f the basal cell layer has been removed (2) myriads of yellowish macules less than 0.5 mm. in diameter dicat that the upper dermis has been reached, making the pilosebaceous apparatus vis ble (3) as planing goes deeper th surface appears studded with yellowish lobulated papules wh ch are the sebaceou glands that hav been cut er and s the depth usually achieved in moderately deep planing (4) if planing s carried deeper decided resi tance f the tis es is encountered, primarily because the tissue is below the penetration of f eezing (about 2 mm.) If freezing done again at this le el further depth can be ach ved with relati ease, but caution is in order (5) If planing is carried still deeper yellow nubbins which are lobules of subcutaneous fat, are exposed. This level is well below the sebaceous glands and at the depth of the deepest hair pa pillae. Planing at this level is likely to result in removing so much adnexa as t cause scar formation.

Results of experiments on the comparative effects of refrigerant on animal and human skin ndicate that human facial skin can tolerate considerable freezing with ethyl hloride or dichlo otetrafluoroethane (Freon 114) but that mixtures containing large proportions of the much colder d hl rodifluorometha e (Freon 12) may be undesirable. R freezing an area of the skin to perform more adequate plan g not considered hazardous

One of the authors performed five full f ce plan g on 3 patient with pitted acne scars who had typical keloids elsewhere on the body In each, a small test area was first planed on the fac then, no u toward reaction having occurred in 6 weeks the full face was planed All 3 patients had an en tir l satisfactory course over many months after planing

* [It is encouraging to learn that patients with acne scarring and keloids elsewhere on the body apparently may ha their face planed without formation of keloids in that area. Of course, much additional experience in this regard is necessary —Ed]

Dermabrasion Tattooing Preliminary Report is presented by Frank D Bernard[8] (Univ of Wisconsin) The technic is used in treatment of port wine stain hemangiomas.

METHOD.—Under general anesthesia an Iverson dermabrader is used to remove the superficial layers of the epithelium Dermabrasion is carried only sufficiently deep to produce a denuded area to receive pigment Bleeding is controlled by warm saline packs and pressure While pressure is being applied the pigment is carefully mixed to obtain a good color match. The pigment is suspended in saline to form a paste and when the denuded area is free of significant bleeding this preparation is applied evenly and rather heavily Fine mesh gauze followed by application of a pressure dressing completes the procedure The dressings are allowed to fall off as the denuded surface heal

Results in a small series have been sufficiently good to warrant further trial In some cases most of the lesion was covered by a permanent pigment layer with marked improvement Complete coverage of the hemangioma has not been achieved and probably never will be but the improvement gained allows the patient to disguise the lesion with a minimum of ordinary cosmetics Before the procedure can be advocated for general use the technic must be further developed so that the take of the pigment is more uniform Factors believed to influence the degree of take include depth of the lesion amount and character of the postoperative exudate on the wound surface depth of dermabrasion and amount of postoperative motion in the treated area.

► [When referring to the therapy of "port wine stain in the introductory paragraph the author states, Application of radioactive material raises serious objection In our opinion this statement requires clarification While radium and superficial x-rays are contraindicated in the therapy of this condition, there is one form of radioactive material, i e thorium X to which these objections do not apply Thorium X has been used in dermatologic practice for over 45 years, so that by now there is considerable long term experience with this material One of the principal applications has been in the treatment of these port wine stains When applied according to accepted technics, one can expect favorable cosmetic response in about one third of the patients treated To our knowledge no sequelae of any consequence have resulted from the proper use of thorium X in the treatment of nevus flammeus —Ed]

Note on Treatment of Epitheliomas by Dermabrasion C. M Ridley[9] (London Hosp) treated 11 patients 2 of them with radiodermatitis. Initial results were successful The area planed included a margin of 2 5 mm normal skin In some cases 2% Xylocaine with 1 80 000 epinephrine was

(8) Plast & Reconstruct Surg 22 267 270, September 1958
(9) Brit. J Dermat. 70 293-295 Aug Sept 1958

used as a local anesthetic instead of Arcton or Freon spray. This made it easier to judge when small neoplastic areas had been adequately removed.

One patient with radiodermatitis had been treated 3 years previously with x-rays for basal cell carcinoma in the lumbar region. An ulcer with a raised edge in the center of the area of radiodermatitis proved to be basal cell carcinoma histologically. Further x-ray treatment was not feasible and excision would have meant extensive intervention and grafting. The other patient with radiodermatitis had had x-ray and radium treatment for keratoses and epitheliomas of the face. A triangular area involving the whole left side of the upper lip was particularly affected, the skin showing atrophy, pigmentation, telangiectasia, multiple small keratoses and a dome-shaped basal cell carcinoma. After 3 dermabrasion treatments the skin healed completely.

If there is no late recurrence the treatment will substitute 3 sessions of mild inconvenience for hospitalization, general anesthesia and extensive surgery. The rate of healing was not significantly slower in areas of radiodermatitis than in other areas. The healed areas were smooth and atrophic and less pigmented than before. Healing was a little slower in 2 cases of intraepidermal carcinoma on the external ear than in other lesions but ultimately the skin was sound and no scarring was apparent.

► [For obvious reasons it will not be possible to judge the efficacy of this unorthodox form of therapy until at least a 3-5 year period of observation has elapsed.—Eds.]

New Treatment for Pitted Scars: Preliminary Report is presented by Arthur S. Spangler (Harvard Med. School).

PROCEDURE.—The area of scarring is anesthetized with 2% procaine solution, using a 20-gauge needle. A triangular 2-edged, Bowman [illegible] needle is inserted through the hole made by the procaine needle, and the fibrous strands beneath the scar are cut by horizontal motions of the knife. After bleeding has been partially controlled by pressure, approximately 0.1 cc. of a suspension of fibrin foam (17 mg./cc.) is injected into the area beneath the scar. The injection is made with a 20-gauge needle inserted through the opening made by the procaine injection. The opening is then partially closed by pressure and covered with adhesive tape.

A total of 23 patients with 253 deep-pitted scars were treated. An average of 0.1-0.[illegible] cc. suspension was used d

pending on the size of the scar Results were uniformly good in obliterating depressions There has been no recurrence of pitting in 74 scars treated with a single injection and observed 24 months. Scars deep enough to cause loss of pilosebaceous orifices and atrophy of the epidermis remained visible because of contrast with surrounding normal skin but were much less conspicuous than previously

Most patients experienced no discomfort Rarely slight aching or mild stinging was experienced but symptoms were promptly relieved by 10 gr acetylsalicylic acid. There have been no serious side effects such as infection keloid formation or foreign body granuloma.

► [The photographs in the original article show a very significant improvement in the appearance of the scarred areas. However until more experience has been gained, one cannot rule out the possibility that a foreign body reaction might develop in the skin of some patients —Eds.]

Chondrodermatitis Nodularis Chronica Helicis Nondeforming Surgical Cure for Painful Nodule of Ear is described by Murray C Zimmerman[2] (Univ of Southern California) The operation was devised on the assumption that the basic pathologic changes are primarily in the cutis. They are secondary (if present at all) in the perichondrium cartilage or epidermis It is postulated that these changes are the result of chronic scarring from actinic or mechanical trauma This binds together the epidermis cutis and perichondrium into a firm unit Further trauma leads to edema in the bound-down area, with resultant pressure induced ischemia and possibly ischemic neuritis

The surgical approach has four aims (1) to cut the old adhesions which firmly bind down the epidermis and cutis on the perichondrium (2) to eliminate the mechanical squeezing of the dermis between perichondrium and epidermis leading to ischemic change, (3) to remove existing reactive inflammatory tissue in the cutis perichondrium cartilage and epidermis at the chondrodermatitis site and (4) to cut the sensory nerves supplying the area for immediate relief of the characteristic pain

The surgical procedure is quick and easy and leave no postoperative deformity It can be done in one stage The author has treated 13 patients with no recurrences The only complications have been a small hematoma in 1 case and

(2) A.M.A. Arch Dermat 78 41-46, J ly 1958

temporary oozing at the incision site in another No postsurgical chondritis or secondary infection has occurred.
► [The original article contains detailed and illustrated description of the technic —Eds]

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2 ECZEMATOUS DERMATITIS (INCLUDING ALLERGIC) INDUSTRIAL DERMATITIS ATOPIC DERMATITIS URTICARIA

Lichenoid Eruptions Following Contact Dermatitis were observed by William R. Buckley[8] (Univ of Rochester) in photographic operators handling certain p-phenylenediam mes These aromatic mines are used as color developers in the photographic trade and in making chemical intermedi tes dyes for furs and antioxidants for gasoline and rubber

Contact dermatitis from exposure to aromatic amines in th photographic ndustry may be acute or subacute. In the acut type an intense eczematous response occurs that show histologically liquefaction of the basal layer in ad d tion to the usual features of dermatitis. On subsidence of the cute erupt on the residual lesions are lichenoid in type. In the bacute type wh ch accounts for over 90% of the cases bserved dry papular lesions develop slowly and are u ually lichenoid from the beginning If contact with the mi e ufficiently great or prolonged, the subacute proc ess may vol e nto the acute variety A reddish purple or iolaceous color is present throughout the acute or subacute skin reaction. Although the dry papules of subacute derma titi nd healing acute eruptions resemble lichen planus clin call nd histologically most microscopic sections show pott parakeratos s and a mor intense perivascular and d ermal infiltrate than is noted in true lichen planus. Pigmentary hanges occur in the skin as healing of lichenoid eruption continues S h ha ge ha e not been permanent but may tak a ear or more for complete clearing in dark complexioned persons.

Lichenoid eruptions after contact dermatitis occu only in sensiti ed persons. The hydrochloride salt of the substituted p-phenylenediam es when applied to the kin of a sensitized

(8) A M A Arch Dermat 78 5 37 October 1958

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Most patients experienced no discomfort. Rarely slight aching or mild stinging was experienced but symptoms were promptly relieved by 10 gr. acetylsalicylic acid. There have been no serious side effects such as infection, keloid formation or foreign body granuloma.

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Chondrodermatitis Nodularis Chronica Helicis: Nondeforming Surgical Cure for Painful Nodule of Ear is described by Murray C. Zimmerman[2] (Univ. of Southern California). The operation was devised on the assumption that the basic pathologic changes are primarily in the cutis. They are secondary (if present at all) in the perichondrium, cartilage or epidermis. It is postulated that these changes are the result of chronic scarring from actinic or mechanical trauma. This binds together the epidermis, cutis and perichondrium into a firm unit. Further trauma leads to edema in the bound-down area, with resultant pressure-induced ischemia and possibly ischemic neuritis.

The surgical approach has four aims: (1) to cut the old adhesions which firmly bind down the epidermis and cutis on the perichondrium; (2) to eliminate the mechanical squeezing of the dermis between perichondrium and epidermis, leading to ischemic change; (3) to remove existing reactive inflammatory tissue in the cutis, perichondrium, cartilage and epidermis at the chondrodermatitis site and (4) to cut the sensory nerves supplying the area for immediate relief of the characteristic pain.

The surgical procedure is quick and easy and leaves no postoperative deformity. It can be done in one stage. The author has treated 13 patients with no recurrences. The only complications have been a small hematoma in 1 case and

(2) A.M.A. Arch. Dermat. 78:41-46, July 1958.

the t x c princpl of philodendron is water soluble and that t l es with n the leaves rather than on their surface.

A paradox in philodendron dermatitis is that t occurs freq ently in worker m nurseries but seldom in housewives who handle the plants at home. This probably can be ex plai ed by the fact that plants n the home are rarely touched, whereas nursery workers may come in contact with cut lea es and stems hundreds of times a day Further in the home plants are watered at the base to avoid dripping and plashing but in a nursery they are watered so that the entire plant becomes wet.

► [Other cases of philodendron dermatitis, including several in house ives, ere reported by Ayres and Ayres (A M A. Arch Dermat. 78 330, 1958) The reasons given by Dorsey explain why nonoccupational dermatitis due to this very common plant apparently is relatively rare — Eds]

Identical Skin Eruption in Five Men after Massive Exposure to Jellyfish (Aurelia) Aurelia, or the saucer blubber usually does not cause injury to the skin when handled. However Hanns Pacy[3] (Tea Gardens, New South Wales) report the multaneous ppearance of an itchy papulovesicular eruption on the feet and ankles of 5 adult brothers 16 hours after contact w th hallow water massively nfested with a j llyfish seemingly of the genus Aurelia. The papules were sharply defined, arising out of unaffected skin pink in color and 4-8 mm in diameter In the center of the larger lesion were small esicles containing serous fluid. Internal and external a tih taminic treatment relieved the pruritus the 3 more severely affected brothers, but did not affect the 8-day course f the disease as compared with 2 controls treated with calamine lotion only

St ngs f the larger jellyfish, such as physalia (bluebottle) r brown blubbers, re usually noticed immediately but these men noticed nothing until they awoke the morning after contact. The larger jellyfish stings are painful but pain wa enti ly bsent in these men. The brothers all reported they had experienced similar eruptions 2 years previously after posure to milar jellyfish whi h massively infested shallow water At that time the lesions lasted about 5 days.

Contact Dermatitis Due to Thermofax Copy Paper Junji H segawa, F ed Levit and Samuel M Bluefarb[4] (Chicago)

(M J Australia 146 182, Oct 19 1957
J M A 166 23, Mar 8 1958

operator will produce an eruption that duplicates the lesions seen clinically. The patch test is removed in 24 hours and the underlying skin is washed gently with an acid type skin cleaner to remove excess chemical which because of its proclivity to become fixed to epidermal cells might lead to sensitization by the patch test itself.

Preventive measures to control contact dermatitis in the photographic industry include (1) proper selection of operators avoiding those with chronic skin disorders (2) proper training in handling of chemicals and good housekeeping in work areas (3) avoidance of actual contact with chemicals by use of mechanized chemical processing equipment, rubber gloves and aprons (4) removal of the chemicals from the skin as soon as possible and (5) prompt medical attention to operators who have had considerable skin contact with substituted p-phenylenediamines.

► [Neither allergic contact dermatitis due to p-phenylenediamine and other aromatic amines nor lichen planus and lichenoid eruptions which resemble lichen planus are rare. What i unusual is the high incidence of lichen planus-like eruptions in a group of workers with allergic contact dermatitis due to thi particula group of chemicals. Buckley does not identify the exact p-phenylenediamine compounds used in the plants that he investigated. It i interesting that apparently one or several of these compounds have the capacity to produce lichen planus like eruptions —Eds.]

Philodendron Dermatitis. Clete Dorsey[4] (Univ of Southern California) reports a case.

Mexican girl 23 worked in a commercial greenhouse. A papulovesicular eruption involving the dorsa of both hands, inner wri t and forearms and outer surfaces of the upper arm tarted 2 week after she began planting philodendron cuttings. Her eyel l face and neck were diffusely swollen and erythematou. A pat h test wa negative after 24 hours, but when the crushed leaves nd sten used for testing were moistened with water the test became pos ti e at 48 hours. Patch tests with other plant handled by the patient wer negativ.

Three other persons worked at the nur ery where the patient was employed. The owner and hi wife were allergic to philodendron but a Mexican gardener wa n t. Of (other commercial nursery owners who were inter iewed 2 reported a high incidence of philodendron sen itivity among their workers. They reported that the plants were m re trou blesome when the leaves were wet. This ob ervati n plus the fact that the present patient showed a p itive pat h test reaction only after the leaves were m t tened ugge t that

(4) California Med. 88:329-330, April, 19 8

touch the paper when the hand rests while making notes.

Since there is no known method of desensitization cure can be attained by a change of job or a change of paper Non allergenic papers are now available for one type of machine—Minnesota Mining and Manufacturing Company Thermofax Duplicator papers DPX 12-88-J1 (buff tinted) and DPX 26-36-J10 (white) Exposure to even a pencil contaminated by touching one of the allergenic papers is enough to cause the eruption to relapse, so a complete office changeover to the new paper seems the only solution.

► [Dermatitis due to Thermofax duplicating paper has been reported from many parts of the United States (Standish, M. Connecticut M J 22 363 1958 Cipollaro, A C. A M A Arch. Dermat 77 334, 1958 Kendrick, F J ibid p 334 Domonkos, A N ibid, p 625 Silverberg M G ibid, p 741 and Fisher A A ibid, p 741) It is our understanding that the chemical previously responsible for the allergic contact dermatitis from Thermofax paper has been changed, but sensitivity to this new paper apparently has already been observed.—Eds.]

Eczematous Sensitization to Neomycin and Bacitracin was observed by V Pirilä and T Wallenius[8] (Univ of Helsinki) during a 20-month period in 28 patients on whom the two drugs were used simultaneously in the same ointment. This combination was used in treating infectious eczema in 27 patients and burns in 1

In 25 patients an epicutaneous test was performed with the various components of the ointment used. All 25 responded to neomycin and 18 to bacitracin but none to the ointment base materials. The reactions often developed only 3-5 days after the test which might be due to the poor absorption of the antibiotics through the skin.

Many patients were allergic to neomycin and to bacitracin Such widespread hypersensitivity to two different substances could hardly be considered as a simultaneous, true heterogeneous sensitization against neomycin and bacitracin, particularly as no isolated hypersensitivity to bacitracin alone was observed among the study patients. The hypersensitivity to neomycin was about 10 times stronger than to bacitracin. These observations suggest that the neomycin and bacitracin compounds, available to the authors, might have contained a mutual or closely related substance(s) which caused the sensitization. The existence of such a com

(8) Hautarzt 8 514-519 November 1957

report 2 cases of this one of which is described here.

Man 63 had severe dermatitis of the face, palms dorsum of the hands and wrists which appeared 1 week after he received ? injections of penicillin for an ear infection. A patch test with 5% solution of nickel nitrate was positive. Ten days after leaving the hospital he had a recurrence of the dermatitis. He then recalled using a Thermofax duplicating paper at work for several weeks before the first attack of dermatitis. Patch tests with this copy paper in both its preprocessing and postprocessing state were strongly positive A patch test with a special hypoallergic Thermofax paper was also positive Patch tests with four types of plastic material, potassium dichromate, hatband material basic chromium sulfate bichloride of mercury copper sulfate cobalt nitrate and Remington Rand Transcopy paper were negative.

The Thermofax process uses a particular type of paper which is simultaneously subjected to heat, light and pressure while in close contact with the page being duplicated. After a few seconds exposure a direct positive image is obtained and the copy may be used immediately The allergenic material in the Thermofax paper is reported to be a tertiary butyl catechol compound. The authors patch tested patients with other forms of dermatitis using Thermofax copy paper and obtained negative results

Contact Dermatitis from High-Speed Duplicator Papers New Disease of Office Workers Charles Sheard Jr Herbert J Spoor and Robert Abel[7] (Cornell Univ) report 5 cases The cause is a type of sensitized paper used in a new high speed duplicating machine in which the paper is inserted in the machine along with the sheet to be copied and is exposed to intense light The chemical in the paper is a trade secret, but the authors were informed that it is a simple chemical

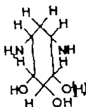
The eruption is severe with vesiculation erythema and seborrhea like superficial scaling It characteristically seems to involve the lower lip a site invariably affected in smokers. Messengers exhibit the eruption on the knuckles where they touch the paper when they carry bundle f it with fingers under the string or on the ulnar forearms or leaned-on areas. Businessmen often have the eruption on the first 3 fingers of both hands where they touch the paper when turning pages and folders or on the ulnar right palm where they

(7) A.M.A Arch Dermat 77 435-437 April, 195

mstances ordinary patch testing was insufficient t elicit a reaction. However light scarification of the area before test ing regularly yielded positive results in sensitized patients.

Neomycin, obtai ed from Streptomyces fradiae is a m x ture of neamine and two glucosides of this ubstance

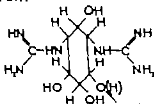
NEOMYCIN



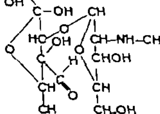
NEAMINE BIOSAMINE

F 3 (Courtesy of Bab, E et al J Invest Dermat 30 225 231, M 58.)

STREPTOMYCIN



STREPTIDINE



STREPTOBIOSAMINE

F urtesy of Bab, E et al J Invest Dermat 30 22 23 May 1958)

Framycetin a closely related antibiotic, is another neamin gluco ide The common neamine mo ety is a cyclohexane be ring tw mino groups (F g) The glucide fractions f neomycin B and C and framycet n are probable bioses heari g a am no group The formula of streptomycin (Fig) lso con sts of a substituted cycloh xan (t eptidin) linked t an amino-substituted biose (streptobiosamine)

mon component i quite possible The neomycin compound consists of three components neomycin A B and C the relative amount of each component varying with the different neomycin preparations. Furthermore the preparations also contain some contaminants The composition of bacitracin is not yet clarified According to Jawetz bacitracin preparations sold in the United States contain abont 20% contaminants

► [Since allergic eczematous contact sensitization to bacitracin alone is very uncommon the most reasonable assumption would be that neomycin was the primary allergen in these cases with secondary (cross-) sensitization to bacitracin. This would presuppose that immunochemically identical or similar groupings are present in neomycin and bacitracin, unless the contaminant mentioned by Pirila and Wallenius play a role Further support comes from a publication by Niel Hjorth on overtreatment dermatitis due to neomycin bacitracin ointment (Ugesk. laeger 120 1323, 1958) He also reported a high incidence of sensitization to both neomycin and bacitracin.

It is puzzling that, to our knowledge even though number of preparations combining neomycin and bacitracin have been sold in the United States for several years, there has been no obvious increase in sensitization to this combination of antibiotics —Ed]

Cross-Sensitization between Neomycin and Streptomycin. *During the first year of use of neomycin Edwin Sidi, Marc Hincky and Robert Longueville*[9] (Paris) observed no sensitizations Only after reapplication of neomycin in patients treated with it several months previously did a number of cases of sensitization appear During investigation of a case of eczema due to contact with neomycin it was found that the patient had become extremely sensitive to streptomycin As this patient had had no previous contact with streptomycin it was decided to test all further patients sensitized to neomycin or streptomycin with both compounds. It was found that patients sensitized to either one are regularly sensitive to the other

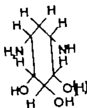
To date 8 such cases have been observed Five of the patients with positive patch tests to both antibiotics had never had contact with streptomycin Two had no known contact with neomycin but had been handling streptomycin One patient had contact with both antibiotics and reacted with an anaphylactoid response to an intramuscular injection of streptomycin followed by eczematization of neomycin treated areas. In every case reaction to streptomycin was markedly more positive than to neomycin In a number of

(9) J I nvest. Dermat. 30 225-231 May 195

nstances, ordinary patch testing was insufficient to elicit a reaction However light scarification of the area before test ing regularly yielded positive results in sensitized patients.

Neomycin, obtained from Streptomyces fradiae is a mixture of neamine and two glucosides of this substance.

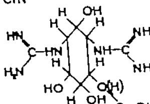
NEOMYCIN



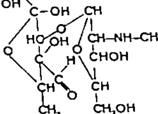
NEAMINE BIOSAMINE

F (Courtesy of Sch. E. et al. J Invest. Dermat. 30 225 231. M 958.)

STREPTOMYCIN



STREPTIDINE



STREPTOBIOSAMINE

(Courtesy of Sch. F. et al. J Invest. Dermat. 30 225 231, May 1 58.)

Framycetin, a losely related antibiotic, is another neamine gl de The common neamine moiety is a cyclohexane bearing two mino groups (Fig 2) The glucide fractions d eomycin B and C and framycetin are probable bioses bearing ammo group. The formula of streptomycin (Fig 3 ls con ts f substituted cy lohexane (streptidine) l ked to an amino-substituted biose (streptobiosamin)

The chemical configuration causing cross sensitization between neomycin and streptomycin is likely to be found in the aglycone moieties but the exact chemical group responsible for this phenomenon has not been ascertained.

The type of reaction seen after topical sensitization to antibiotics seems somewhat different than that in the usual allergic contact dermatitis. Instead of an acute vesicular oozing process the reaction is often of the dry desquamative spreading type which may at times involve covered areas more suggestive of atopic dermatitis. The necessity for scratching the skin area to be patch tested to obtain reproducible results seems to indicate a deeper site of reaction than in the usual contact dermatitis.

► *[The following facts concerning allergic sensitization to neomycin have come to be recognized recently (1) Sensitization to this antibiotic is not particularly uncommon. (2) Cross sensitization to streptomycin and perhaps also to bacitracin is not uncommon. (3) Allergic sensitization sometimes cannot be demonstrated with the conventional patch test in such instances, intracutaneous tests for the delayed 48-hour reaction (Epstein S Dermatologica 115 596, 1957) or patch-on-scratch test are necessary to show the existence of allergic sensitization (4) Clinically allergic sensitization to neomycin can become manifest either as a subacute erythemato-squamous or an acute papulovesicular eruption —Eds]*

Persistence of Allergic Eczematous Sensitivity and Cross-Sensitivity Pattern to Paraphenylenediamine. Paraphenylenediamine (PPD) is a frequent and potent sensitizer producing many cases of allergic eczematous contact dermatitis *It is used principally in hair and fur dying It may cross react with other chemicals having an amino grouping in the para position in the benzene ring including certain dyes local anesthetics para aminobenzoic acid (PABA) and the sulfonamides*

Alexander A Fisher Alfred Pelzig and Norman B Kanof[1] (New York Univ Post Grad. Med. School and Skin and Cancer Unit) found that 46 of 50 patients with strong hypersensitivity to PPD retained this sensitivity for 3 10 years *Of the* 46 PPD reactors *11 gave cross* reactions to benzocaine 4 to procaine and benzocaine *3 to PABA and benzocaine and 1* to sulfanilamide

Several PPD positive women in this study repeatedly exposed themselves to PPD in hair dyes without any increase in PPD sensitivity as measured by patch test The exposures always caused a severe dermatitis but these patients

(1) J Invest. Dermat. 30 9-12, January 1958

showed no widening of their spectrum of sensitivity Repeated patch testing of these PPD-positi e patients with other compounds contain ng the para-aminobenzyl group did not sensitize them to the other compounds

The tudy indicates that PPD sensitivity once established, persists for years. The spectrum of cross-sens tivity to I PD appears to be related to an individual host factor and to be established early

► [The persistence of PPD sensitivity in 46 of 50 patients is in conformity rth current knowledge Allergic eczematous sensitivity to certain other allergens (g nickel), according to reports published in recent years, is apparently more eadily lost. The new finding in these studies is that there was no widening of the cross-sensitization pattern despite repeated exposures to the primary allergen, which were sufficiently intense to produce severe dermatitis well as exposures to potential secondary allergens W believe that more extensive studies on this important problem are indicated.—Eds]

Contact Dermatitis from Vitamin B_1 (Thiamine) Relapse after Ingestion of Thiamine Cross-Sensitization to Co-Carboxylase. Niels Hjorth (F'nsen Inst., Copenhagen) reports a case f occupational dermatitis due to thiamine n a girl 17 Relapses of the dermatitis occurred after ingestion of 200 mg thiam ne and later after intracutaneous njecti n of 10 mg P tch tests with pure crystall ne thiamine were posi ti e e en m 0 1 ℅ dilution

Th thiamine molecule s comprised of a thiazole and a pyrimidine compon nt After ntestinal esorption the thia m ne is esterified w th pyrophosphori acid and thu changed t co-carboxylase which is a coenzyme n cellular metabol m Part of the i gested thiami e s el m nated n the urine a pyrimid ne deri t ve

The decompos tion products have not been tested n any f th p evious l reported cases of hypersensitivity to thia m ne Sen tizatio t these product m ght occur ine thia m n tabl at th p ailing pH of the kin urface l at h test w th th thiazol component of thiamine were negat l at h test with the pyrimidin component pu e nd n 10% sol tion, w r pos ti e on on occa io but tests w tl 10% and 1 ol tio were negati e 2 day later As thiam ne elicited eaction even in 0 1% solution, it s unlikely that the decomposition products could be the primary llergen.

The chemical configuration causing cross sensitization between neomycin and streptomycin is likely to be found in the aglycone moieties, but the exact chemical group responsible for this phenomenon has not been ascertained.

The type of reaction seen after topical sensitization to antibiotics seems somewhat different than that in the usual allergic contact dermatitis. Instead of an acute vesicular oozing process the reaction is often of the dry desquamative spreading type which may at times involve covered areas more suggestive of atopic dermatitis. The necessity for *scratching the skin area to be patch tested to obtain reproducible results* seems to indicate a deeper site of reaction than in the usual contact dermatitis.

► [The following facts concerning allergic sensitization to neomycin have come to be recognized recently (1) Sensitization to this antibiotic is not particularly uncommon (2) Cross sensitization to streptomycin and perhaps also to bacitracin is not uncommon (3) Allergic sensitization sometimes cannot be demonstrated with the conventional patch test in such instances, intracutaneous tests for the delayed 48-hour reaction (Epstein, S *Dermatologica* 115 596 1957) or patch-on-scratch tests are necessary to show the existence of allergic sensitization (4) Clinically allergic sensitization to neomycin can become manifest either as a subacute erythematosquamous or an acute papulovesicular eruption —Eds.]

Persistence of Allergic Eczematous Sensitivity and Cross Sensitivity Pattern to Paraphenylenediamine Paraphenylenediamine (PPD) is a frequent and potent sensitizer producing many cases of allergic eczematous contact dermatitis. It is used principally in hair and fur dying It may cross-react with other chemicals having an amino grouping in the para position in the benzene ring including certain dyes local anesthetics para aminobenzoic acid (PABA) and the sulfonamides

Alexander A Fisher Alfred Pelzig and Norman B Kanof (New York Univ Post-Grad. Med School and Skin and Cancer Unit) found that 46 of 50 patients with strong hypersensitivity to PPD retained this sensitivity for 3-10 years. Of the 46 PPD reactors *11 gave cross reactions to benzocaine* 4 to procaine and benzocaine 3 to PABA and benzocaine and 1 to sulfanilamide

Several PPD positive women in this study repeatedly exposed themselves to PPD in hair dyes without any increase in PPD sensitivity as measured by patch tests The exposures always caused a severe dermatitis but these patients

(1) J Invest. Dermat. 30:9-12, January 1958.

showed no widening of their spectrum of sensitivity Repeated patch testing of these PPD-positive patients with other compounds containing the para-aminoben yl group did not sensitize them to the other compounds.

The study indicates that PPD sensitivity once established, persists for years. The spectrum of cross-sensitivity to PPD appears to be related to an individual host factor and to be established early

► [The persistence of PPD sensitivity in 46 of 50 patients is in conformity ith current knowledge. Allergic eczematous sensitivity to certain other allergens (g nickel), according to reports published in recent years, is apparently more readily lost. The new finding in these studies is that there was no widening of the cross-sensitization pattern despite repeated exposures to the primary allergen, which were sufficiently intense to produce severe dermatitis as well a exposures to potential secondary allergens W belie that more extensive studies on this important problem are indicated.—Eds]

Contact Dermatitis from Vitamin B_1 (Thiamine) Relapse after Ingestion of Thiamine Cross-Sensitization to Co-Carboxylase. \ els Hjorth[2] (Finsen Inst., Copenhagen) reports a case of occupational dermatitis due to thiamine in a girl, 17 Relapses of the dermatitis occurred after ngestion of 200 mg thiamine and later after i tracutaneous injection of 10 mg Patch tests with pure crystalline thiamin were posi t e, en in 0.1 % dilution.

The thiamin molecule is comprised of a thiazole and a pyrim d n component After intestinal resorption the thiamine is esterified with pyrophosphoric acid and thus changed t co-carboxylase which is a coenzyme in cellular metabol sm Part of the ingested thiamine is eliminated n the urine a pyrim d ne deri ative.

Th decomposition products ha e not been tested any f the pre io l eported cases of hypersensitivity to thiamine Sen tiz tion to these products m ght occur since thia e un t bl at the prevailing pH of the skin urfa l tch test w th th thiazole component of thiam n wer eg t I at h test w th the pyrimidine component pu e d 10% solution, wer positive on one occa ion, but tests w th 10% a d 1 solution were negati e 2 day later As thiam n elic ted reactions even n 0.1% solution, it i unlik ly that the decomposition products could be the primary llergen

[2] Acta Dermat 38:341-344, M 1 58

Though the pyrimidine derivative used for the tests (2 methyl-6-amino-5-brom methyl pyrimidine) is a primary irritant, the reactions provoked by it might be an expression of a cross sensitization or secondary allergy provided the pyrimidine part was the antigenic determinant group of the thiamine molecule This cross sensitization in that case should occur with amino-methyl pyrimidine However tests with this compound were negative. Thus the observed reactions with the pyrimidine component of thiamine must have been due to the primary irritant properties of the substance and it may be concluded that the primary allergen in this case was the whole thiamine molecule. A secondary allergy to co-carboxylase was indicated by positive patch tests to 10% and 1% dilutions This seems to be the first demonstration of a hypersensitivity to a pure coenzyme.

► [The first demonstration of allergic hypersensitivity to a coenzyme but only one of many now known allergic sensitivities to body-own substances. The question arises why this patient remains clinically well when she is exposed to exogenous thiamine from food as well as exposed uninterruptedly to thiamine from her endogenous co-carboxylase. The answer in all probability lies in the fact that even in allergic hypersensitivity the size of the exposure is an important factor There is simply not enough thiamine available from food and coenzyme to elicit a clinically recognizable reaction in the skin.—Eds]

Local Allergic Edema Induced by Injected Procaine Diagnostic Value of 24-Hour Intracutaneous Test. Sheppard Siegal[3] (Mount Sinai Hosp New York) observed 3 patients who had repeated reactions to procaine characterized by *marked swelling of the cheek and face at the site of injection* of the drug for dental anesthesia There was no evidence of general reaction or urticaria. In each instance a preliminary impression of infection or trauma as a cause of the edema had to be discarded Allergy to procaine was demonstrated by a skin test reaction of the *delayed 24-hour* type to intracutaneous injection of the drug In each case skin tests with monocaine were also positive Skin tests with Xylocaine were negative. *The latter anesthetic is sufficiently distinctive in chemical structure so that cross sensitization is unlikely* It is a safe substitute for procaine

The phenomenon of local allergic edema due to injected procaine is not widely recognized. Although procaine has been in use for over half a century reports of this type of al

(3) J Allergy 29:329-335 July 1958

lergic reaction have appeared only in recent years. Such reactions may be more frequent because of the widespread use of procaine penicillin since 1948. This slowly absorbed depot preparation contains procaine in 12% suspension and may be a more potent sensitizer than the usual procaine solution. This possibility is suggested by a concomitant positive penicillin 24-hour type skin test in 2 of the 3 patients with procaine edema. Two other patients with penicillin allergy were shown to have a positive 24-hour skin test with procaine.

► [This study provides a reasonable explanation for local reactions to procaine which are not too unusual and which hitherto have been unsatisfactorily interpreted as due to "infection." Further, it presents a practical technic for establishing whether delayed procaine sensitivity exists in a patient. The lack of cross-sensitization between Xylocaine and procaine on intradermal testing parallels the finding in allergic eczematous sensitivity to procaine.—Eds.]

Allergic Origin of Zirconium Deodorant Granulomas was demonstrated by Walter B. Shelley and Harry J. Hurley[4] (Univ. of Pennsylvania). A standard commercial zirconium stick deodorant was rubbed in the left axilla for 5 minutes every morning by 30 men. After 1 month a chronic noninflammatory eruption appeared in the axilla of 1 man. Two weeks later biopsy showed an early epithelioid granuloma. At 10 weeks biopsy showed a fully formed granuloma of many epithelioid cells, some giant cells and a few inflammatory round cells. The right axilla of all subjects was treated at the same time with a stick identical with the deodorant stick except for the absence of zirconium. No gross or microscopic changes were observed in any subject as a result of this application. Thus, repeated topical application of stearate, hexachlorophene, carbitol, alcohol and perfume produced no granulomas.

After completion of the foregoing experiment, the subjects applied 0.5% sodium zirconium lactate in sodium stearate alcohol and water to the right axilla for 5 minutes daily for 10 weeks. Sodium zirconium lactate 10% in sodium stearate, alcohol and water was applied to the left axilla. One subject exhibited typical granulomatous changes in the axilla treated with the 10% concentration after application for 1 month. Thus, sodium zirconium lactate in a plain sodium stearate soap vehicle can produce the typical granulomatous

4 Brit. J. Dermat. 70:3 101, March, 1958

response which was observed clinically after use of deodorant sticks containing zirconium

Patch tests with zirconium deodorant were uniformly negative in the 2 men with axillary granulomas and in 20 normal controls However with intradermal testing the men with axillary granulomas showed a unique granulomatous response to the introduction of dilute aqueous solutions of sodium zirconium lactate All areas of skin were reactive. The controls showed no response. Injections of zirconium chloride and zirconium nitrate were as granulomagenic as injections of sodium zirconium lactate in the subjects with positive tests whereas injections of beryllium sulfate and colloidal silica produced no response. It is thus apparent that the 2 men who acquired deodorant granulomas in the experimental studies had a specific hypersensitivity reaction to the zirconium which manifested itself as a granuloma. In 1 of these intradermal injection of 0 02 ml. of 1 10 000 zirconium solution produced a granuloma In the other 0 02 ml of a 1 1000 dilution caused a reaction

In another subject, not part of the experimental study the authors observed acquisition of zirconium hypersensitivity Initial tests for zirconium were repeatedly negative. Months later the test sites showed a granulomatous reaction Further tests with zirconium proved that the subject had become specifically sensitive to zirconium

Patch tests with zirconium stick deodorant were negative in 4 patients who had clinically typical deodorant granuloma of the axillae from use of zirconium deodorants. All 4 were sensitive to intradermal injection of 0 02 ml of 1 1000 sodium zirconium lactate and 3 were sensitive to a 1 10 000 dilution

Though certain granulomas have been suspected of being allergic in origin this is the first direct demonstration in man that the introduction of extremely small amounts of a pure substance may produce a delayed allergic reaction in the form of an epithelioid granuloma. This is an entirely new facet of immunologic response that must be explored in relation to all granulomatous processes Intradermal skin testing must extend to discover and identify granulomagenic allergens which may be operative in such diseases a lepro y sarcoidosis and tuberculosis. Intradermal skin testing of pa

tients with beryllium, silicate and tattoo granuloma should afford rapid demonstration of specific hypersensitivity to the causative element.

The quantitative aspects of the allergic granuloma are of a new order of magnitude. Unbelievably small amounts of zirconium may elicit a granuloma. As little as 0.2 µg sodium zirconium lactate was able to produce a small but grossly visible skin lesion in 1 patient. In the search for the cause of granulomatous disease agents such as fatty acid which are needed in milligram quantities to produce granulomas need no longer be looked for. Instead, agents which act in microgram quantities must be sought. The sensitized patient can respond to traces of an allergen well beyond the point which can be detected by present-day physical and chemical analytical procedures. This accounts for the failure of previous workers to demonstrate zirconium in axillary granuloma specimens.

These studies indicate that the granulomatous response is due to the zirconium ion and not to any particular salt or to impurity. No cross-sensitization phenomena have been encountered as yet, but the possibility of cross-sensitivity to other elements such as its twin hafnium must be borne in mind.

► [These studies confirm what had been suspected clinically, namely that the zirconium in stick deodorants [illegible] the cause of the axillary granulomas seen in the United States in 1956-57. However, probably not all cases can be explained on this basis since some patients with axillary granulomas denied having used one of these sticks.

That these granulomas are of allergic origin is most interesting and also explains why only relatively few among the multitudes who used zirconium-containing deodorant sticks developed granulomas. The finding of granulomatous response histologically does not come as a surprise. The early histologic response at the intradermal test site in the tuberculin type of allergy [illegible] composed mainly of mononuclear cells, but after weeks and months epithelioid cell formation is observed. It appears possible [illegible] that if Epstein (A.M.A. Arch. Dermat. 73:326, 1956) had examined histologically sites of delayed dermal reaction to nickel and chromate after several months he would have encountered similar granulomatous changes. Granulomatous alterations of allergic origin occurring after [illegible] positive patch test with beryllium sulfate in beryllium disease were previously reported by Sheldon (Brit. M. J. 1:1449, 1935).—Eds.]

Asbestos Granulomas and Warts. P. Vulcan and St. Tanasescu[1] report a case.

Woman, 48, worked in an asbestos spinning mill for 5 years. For the last 2 years she had pulmonary symptoms due to inhalation of asbestos

(1) Dermato-venerologia 3:21, Jan.-Feb., 1958.

respon e which was observed clinically after use of deodorant sticks containing zirconium.

Patch tests with zirconium deodorant were uniformly negative in the 2 men with axillary granulomas and in 20 normal controls However with intradermal testing the men with axillary granulomas showed a unique granulomatous response to the introduction of dilute aqueous solutions of sodium zirconium lactate All areas of kin were reacti e. The controls showed no response. Injections of zirconium chloride and zirconium nitrate were as granulomagenic as injections of sodium zirconium lactate in the subjects with positive tests, whereas injections of beryllium sulfate and colloidal silica produced no response. It is thus apparent that the 2 men who acquired deodorant granulomas in the experimental studies had a pecific hyper ensitivity reaction to the zirconium which manifested itself as a granuloma. In 1 of these, intradermal injection of 0 02 ml. of 1 10,000 zirconium solution produced a granuloma in the other 0.02 ml. of a 1 1000 dilution cau ed a reaction.

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Granulomatous alterations of allergic origin occurring after positive patch test ith beryllium sulfide in beryllium disease wer previousl reported by Sneddon (Brit. M. J. 1:1448, 1955) —Ed.]

Asbestos Granulomas and Warts. P. Vulcan and St. Tanasescu[1] report a case.

Woman, 48, orked in an asbestos spinning mill for 5 years. For the last 2 years she had pulmonary symptoms due to inhalation of asbestos

(1) Dermato-venerologia 3:31, Jan.-Feb., 1958.

dust. Six months previously she had injured her right hand. The wound healed within 2 months but a small firm, hyperkeratotic nodule formed at the site of injury. At about the same time, several small wartlike lesions appeared on the dorsal surface of the fingers.

Biopsy of the nodule on the internal margin of the right hand revealed acanthosis and hyperkeratosis of the epidermis with areas of pseudoepitheliomatous hyperplasia. There was an infiltrate in the der

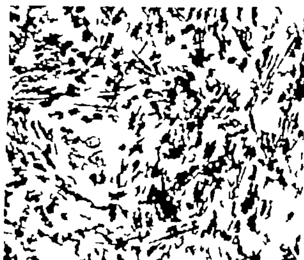


Fig 4.—Histio-fibroblasto-epithelioid infiltration with many asbestos crystals (Courtesy of V. Ioan, P. and T. [illegible], St. Dermato-venerologia 3 21 Jan Feb 1958.)

mis consisting of histiocytes, epithelioid cells and fibroblasts. Among the cellular elements were needle-like birefringent crystals of varying size occurring singly and in groups (Fig 4).

The granulomatous infiltrate in this case resulted from the presence of minute particles of asbestos in the skin. Asbestos is a hydrated magnesium silicate occurring in the form of soft slightly elastic threads. Cutaneous granulomas may result from penetration of the skin by amorphous or crystallized silicon hydrated magnesium silicate aluminum silicate (kaolin) or complex polysilicates (mica feldspar amianthus asbestos). *A variable period of latency usually occurs* between the time of trauma and appearance of a cutaneous nodule.

Examination of 25 women factory workers handling asbestos revealed wartlike lesions in 12. Clinically the lesions resembled simple warts with a predilection for the palmar aspect of the fingers especially at the interphalangeal folds

On biopsy some showed acanthosis and hyperkeratosis w thout evidence of cellular infiltration in the dermis or presence of asbestos needles The authors believe such le- sion result from intraepidermal penetration of asbestos par t cles which are subsequently eliminated without penetra tion of the dermis.

► [The studies of Shelley and Hurley indicate that cutaneous granuloma of this variety may be of allergic origin (see previous abstract) —Eds]

"Chrome Dermatitis Study of Chemistry of Shoe Leather with Particular Reference to Basic Chromic Sulfate presented by George E. Morris (Boston) The physician ttempting to elicit the cause of an eruption of the feet, ha been guided for years by certain accepted dicta (1) that the chromium used in tann ng most shoe leather cannot ause uch eruption because it is not hexavalent and only hexa alent hrom um can cause skin disease and (2) that thi hromium firmly fixed in the leather and cannot be emc ed easily Recent research has demon trated that each of these long taught principles is incorrect.

Leather hem t have established that chrome salts can be leached from shoe leather by the lactic acid and lactate in h man per piratio These salts can thus be deposited on the kin The particul r salt depos ted by the tanning industry in hide fibers and fibrils s bas c chromic sulfate. A repre- sentati e compound of this type the one-third basic chrome li te [Cr(H₂O) OH]SO wa recently made available to the medical profes on for patch testing a wa a chromic la tate complex contam ng lactat ions per atom of tri- l t chromium

F ur cases of shoe-leather dermatitis are reported n which the patients had pos tive patch tests to 0.2% basic chromic llfate Two leather workers who previously had chrome lermatitis also had pos tive tests to this compound. An ther patient had positi e test to sodium dichromate but negative test to basic chrom c sulfate Chemical analysis a nurse s st cking (whose hoes had shown green chro- mium discoloration) evealed la ge quantities of tri alent hromium

Pos ti e patch tests to a trivalent chromium compound ha e not been eported previously Patients ha e been tested

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Biopsy of the nodule on the internal margin of the right hand revealed acanthosis and hyperkeratosis of the epidermis with areas of pseudoepitheliomatous hyperplasia. There was an infiltrate in the der

Fig. 4. Histio-fibroblastic-epithelioid infiltration [illegible] many asbestos crystals. (Courtesy of [illegible] and T[illegible], Br. J. Dermat. [illegible] 3 31 [illegible] Feb. 1958.)

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tion of the skin by jewelry the author patch tested 8 volunteers with metal samples representing the composition of ring jewelry No reactions occurred with pure gold, silver (900 fineness—87.5% silver 2.5% copper pure copper pure nickel, 10-carat gold (9 parts gold, 5 parts copper) nickel silver (75% nickel 25% copper) or silver copper (60% silver 40% copper) However metal corrosion was noted in all cases with pure copper and silver copper and in 1 n tance with silver 900 fineness.

Tests were then repeated with the addition of a sprinkling of table salt (3-5 mg) placed in the central opening of the washer-shaped metal samples. Erythematous and vesicular reactions occurred in 5 patients with silver containing 2.5% coppe in 7 patients with pure copper in 7 patients with sil er copper and in 1 patient with 10-carat gold. One subject showed a delayed follicular erythema when tested with pure gold. The reason for this reaction is obscure as s the paucity of reaction to 10-carat gold In 8 ubjects marked metal corrosion was observed with silver containing copper and with pure copper Such corrosion also occurred in 7 instances with silver copper

It is concluded that in the presence of an adequate concentration of salt a primary irritant is produced when copper or copper alloy in silver is in contact with the skin. Irritation from rings seems commoner than from other metal contacts on the kin. The hands ha e many opportunities for exposure to loose salt, and psychic and thermal sweating can de l er to the ki surface sufficient sodium and chloride ions to atta k metal when concentration results from evaporation A thorough study of jewelry metal might produce al lo fficiently ert to be nonreactive in the presence of a ng salt concentrations on the skin surface.

[In eczematous eruptions involving the ring area, many factor may attribute to the development of the eruption besides the metals in the ring itself Soaps and other detergents, waxes, polishes, oils, chemical cleansers and other substances used in the home or occupation may accumulate under the ring and produce a local eruption, unless the ring is cleaned at regular intervals Gaul investigations demonstrate that salt an be another contributory factor making the metal primary irritant. However the negative patch tests do not entirely exclude the possibility of allergenic action of these metals in Gaul cases As was show by S [illegible], in some cases of allergic dermatitis due to nickel and other compound positive delayed intracutaneous test reaction can be elicited hereas the patch test may be negative —Eds]

with *ammonium or potassium dichromate* (which are hexavalent) chromium acetate, chromium chloride chromium phosphate, chromium carbonate, chromium nitrate, chromium oxide or chromium fluoride The author when looking for the cause of shoe-leather dermatitis found no report in the literature of positive tests to these chemicals. Negative results would be expected since these chromium compounds are not found in shoe leather This is the first report on patients suspected of having shoe dermatitis who were tested with the actual chrome salt found in their shoes.

Case of Contact Allergy to Copper and Zinc is reported by B J Van der Meer[7]

Man 41 a technical worker for the telephone service, had recurrent attacks of eczema, principally on the legs, which responded to ACTH injections and bed rest. He complained of itching in the elbow crease, which was covered with a zinc ointment dressing The next morning this area only was inflamed. In his work he had contact with zinc, but more with copper wire. The ointment contained both zinc oxide and zinc sulfate, and also traces of copper 0.2 or 0 1/1,000.

Three metal plates, 5×5 cm and 1 2 mm. thick, of copper brass and zinc, were applied to the forearm. After 24 hours, a contact dermatitis had developed reaction to copper and brass was severe and to zinc less so but still definite. Patch tests were then made with solutions of zinc sulfate in dilution of 10-1-0 1%, and of copper sulfate, 1-0.1 0 01-0.001 and 0.0001% Zinc produced a reaction with 1% and copper with 0 01% Analysis of the zinc sulfate showed traces of copper of not less than 0 00001% Nickel sulfate 0.5% and potassium bichromate 0.5% produced no skin reaction.

Although the reaction to copper was 100 times as great as to zinc it was concluded that the patient had a true contact allergy to both metals.

► [It would be interesting t know the result of patch tests on this patient with the zinc ointment that was used in the dressing as well as with zinc oxide itself It is difficult to rule out the role f copper contamination of the various preparations used here for patch testing —Eds]

Ring Dermatitis Primary Irritation from Action of Salt on Jewelry Alloys. According to L. Edward Gaul[8] (Evansville, Ind) patients are frequently seen with dermatitis under and around rings or dermatitis of the ear lobes, back, neck chest shoulders wrist or lower abdomen where metal contact presupposes a metal sensitivity In many instances patch tests with metals are negative.

In a search for possible accessory factors related to irrita

(7) Nederl. tijdschr. geneesk 101 2166-2167 Nov. 16, 1957
(8) A.M.A. Arch. Dermat. 77 526-531 May 1 58

Epoxy Resins Their Uses and Chemical and Dermatologic Aspects are described by George E. Morris[1] (Boston) Introduced in 1946 epoxy resins are now widely used in industry With their use have come se ere dermatologic problems, for the chemicals in these resins are sensitizers and irritants. Epoxy resins, chemically known as ethoxylene resins, are polyethers with terminal epoxide groups. Epoxies re available in a wide range of viscosities, from low viscosity liquids to high melting-point solids. Many curing agents and additives used n preparing epoxy resins are severe skin irritant and sensitizers.

The nitial development of epoxies in the Un ted States came from research in the paint industry The qualities of resistan to chemical and to corrosive substances and fumes of durability and of flexibility have resulted in vari ou nd xpanding uses of epoxy-based surface coatings. Epoxies also contain such strong adhesive qualities that they can ffectually b nd together many different materials, incl di g teel aluminum, brass glass plastics, ceram cs, rubber nd wood. Since som epoxies are fluid at room temperatures th y are sed to make parts having thin sections d to fill mold containing fragile inserts. The high insulation resi tance of epoxy resins under extreme relati e humid ty and temperature changes has made them admirably ted for potting and encapsulat g (i.e., sealing of sensiti e lectri parts i pla ti blocks) Besides their importance in the lectri utomotive and a rcraft fields, the over all use of epo es telev sion and electronics is constantly expand g The are also used in the manufacture of nonmetal tool nd d es the field of einforced plastics and in many other du tries

Dermat t es lt ng from contact with epoxy resins is most commonl seen in the central third of the face the nose adjacent area of the heeks upper lip and ey lids. The f earm and hand re lso commonly volved, and some t mes the conjunctiva irritated.

Worker n nd stries u g epoxy esin often are un w e that the re handling chemicals which can irritate the kin Although the main man facturer of epoxies ha e warned of thei dermat logic hazards many workers who

[1] A.M.A. Arch. Dermat. 757 December 5.

Studies in Contact Dermatitis II Lipstick Cheilitis. According to C D Calnan and I Sarkany[9] lipstick cheilitis accounts for more than half the cases of dermatitis due to cosmetics Of 110 cases observed during 4½ years, 98 involved the vermilion border of the lips only The angles of the mouth are usually spared because most women do not apply lipstick to the corners of the lips.

Fluorescein dyes are the only important cause of allergic sensitivity to lipsticks Indelibility cannot be achieved without the use of halogenated derivatives of fluorescein (eosin) The eosin actually combines with the keratin of the stratum corneum Almost all patients with lipstick cheilitis can use a fluorescein free lipstick Such lipsticks are not indelible but are otherwise satisfactory

Occasionally patients with lipstick cheilitis show a negative response to patch tests with eosin in low concentration. This has been used as evidence of localized allergic sensitivity or photosensitivity The authors believe however that such test results are false negatives due to the fact that too little allergen has penetrated the stratum corneum The horny layer on the skin of the back or limbs is moderately thick, whereas that on the vermilion border of the lips is extremely thin. Eosin combines with keratin in an acid pH Hence small amounts of the dye can be immobilized by the keratin of the stratum corneum Only in high concentration will there be enough dye to saturate the keratin and penetrate deeper to react with the antibodies and produce a reaction

Because of false negative patch test reactions with low concentrations patch tests with 50% eosin are recommended Most patients with lipstick cheilitis will have positive reactions to their own eosin-containing lipstick and to 50% eosin and negative reactions to noneosin lipstick. Such patients are advised to use noneosin lipsticks thus avoiding further trouble.

► [Obviously lipstick cheilitis is much more common in London than in New York. Cases of lipstick dermatitis represent only a very small percentage of our patients with allergic cosmetic dermatitis The reasons for this discrepancy in incidence are not immediately evident The finding that indelible fluorescein dyes usually are the cause of these eruptions confirm the original work of Sulzberger and J Goodman (Arch Dermat & Syph. 37 597 1938.) —Eds.]

(9) T St John Hosp. Derm Soc pp 28 36 Winter 1957

Studies of Mechanism of Allergic Eczematous Contact Dermatitis II. Use of C¹ Labeled 2-4 Dinitrochlorobenzene in Guinea Pigs. Victor H. Witten and Cyril H March[3] (New York Univ Post-Grad Med School and Skin and Cancer Unit) used radioactively tagged dinitrochlorobenzene-1 C^{14} (DNC¹ B) to challenge (1) guinea pigs previously sensitized with nonradioactive dinitrochlorobenzene (DNCB) and (2) nonsensitized control animals. Distribution and localization of the allergen or its metabolites in various tissues as evinced by the presence of radioactivity was ascertained by use of the Van Slyke-Steele-Plazin method of carbon combustion and proportional counting

Definite differences in the amount of radioactivity found in sensitized and control guinea pigs after challenge with DNC¹ B were noted in 2 of the 7 tissues studied the skin and the buffy coat layer of the blood. When similar areas were excised from the site of challenge it was found that skin from the control animal contained considerably more radioactivity per milligram than that from sensitized animals. Although no constant differences in the amount of radioactivity present in the regional inguinal lymph nodes nor in the spleen of control and sensitized animals were found, the buffy coat of sensitized animals contained more radioactivity per milligram than that of control animals. No consistent differences were found in the white blood cell counts of sensitized and control guinea pigs. Little or no radioactivity was found in the red blood cells and liver of any of the animal The radioactivity in the serum was somewhat higher and there was no difference between sensitized and control animal

The lesser amount of radioactivity found in the skin of sensitized guinea pigs might result from (1) more rapid loss of radioactivity externally as a result of a more successful effort by the sensitized animal to cast off the allergen from the site of challenge (2) an increased rate of removal of the radioactively tagged allergen internally achieved by the increased vascular lymph and other fluid flow to the site of challenge in the sensitized animal or (3) more rapid removal of the allergen or its degradation products the

(3) J. Invest. Dermat. 1 97 93, August, 1953

actually handle them have not been alerted and, therefore, do not take adequate precautions. Skin contact should be prevented by good plant housekeeping during the addition and processing of these agents. Epoxy resins should be handled only in well ventilated areas although this is not always practicable. Repeated instruction should be given to workers to avoid direct contact with any components used in processing. Workers should be warned to wash off immediately any splatters or spilled material that may come in contact with the skin.

► [As with acrylic resins the more highly polymerized the epoxy resin the lower the incidence of dermatitis. Here is another of the increasing number of agents which are responsible for the rise in the incidence of primary irritant and allergic contact dermatitis among workers. With the advances of science in industry this incidence is likely to continue to increase. It is unfortunate that the advances in our understanding and prophylaxis of the resulting eruptions have not kept pace with the industrial progress.—Eds.]

Sensitizing Structure in Epoxy Resin. L. Edward Gaul[2] (Evansville, Ind.) reports an instance of glue dermatitis traced to epoxy resin. The hardener used was phthalic anhydride. Patch tests were performed with 1% concentrations of the components in olive oil. The patient was sensitive to a sample of air-dried resin but not to heat-cured resin.

The epoxy group was not the sensitizer in this case. Heat curing apparently alters the structure of the resin sufficiently to render innocuous the sensitizing group. Apparently bisphenol A carried the allergenic portion of the resin. A dilution test was positive in 24 hours to a concentration of 0.001% of the resin.

The most important finding is the reaction to the air-dried resin. The patient may have had the sensitizing exposure either because the foreman at the plant added an insufficient amount of hardener or because the substance did not cure long enough. In any event the sample was highly allergenic. This observation suggests a need for awareness of the possibility of epoxy resin sensitization from diverse and unsuspected sources.

► [In these days and times the practitioner must be constantly alert to unsuspected and hidden sources of substances which potentially cause allergic or other reactions, e.g., the epoxy resins, glue, antibiotics in fish, fowl and milk, hormones in capons, etc.—Eds.]

(2) J. Invest. Dermat. 29: 311-313, November, 1957.

ried to thi organ by way of different groups of lymph nodes.

The authors had shown before that sensitization does not subside when the regional lymph nodes are removed after sensitization has been established. Th s would suggest that these lymph nodes are not the only producers of antibodies. Further studies should reveal th nature of the agent which carried n from the regional lymph nodes centripetally and to determin the organs which, besides the regional l mph nodes produce a tibodies and preserve sensitization.

Interference Phenomenon in Allergic Contact Dermatitis. William L. Fpstein and Albert M Kligman[1] (Univ of Pennsyl ania) observed that the simultaneous application of two contact allergens of unequal sens tizing capacity did not result in the expected ncidences of sensitization the weaker allergen wa blocked. Original observations of this inter ference phenomenon were made with two h ghly potent con tact allergens, 2,4-dinitrochlorobenzene and paran trosodi m thyl an l ne The f equency of sensitization to varying ncentrations of each wa worked out over several years in healthy ad lt Negro males. Sensitization rates we within the xpected ra ge wl en the allergens were applied simultaneou ly to separate ites, so long a the concentrations were like or nearly so S multaneou application of unequal oncentrations to separate site however ga e frequency lues f the weaker allergen (paranitrosodimethyl aniline) lecidedl les than expected

Further investigation, using allergen of varying concen t tio and potency establi hed that only potent contact sen t ers can xert interference Stronger allergens can interf re w th weaker ones but not vice versa. The interfering allergen mu t be used at concentration which give maximal rates f sen t atio wherea the allergenic strength of the gent to be blocked mu t be considerably weake In general terferenc seem to be an in tance of competiti e inh bition The tronger allergen p e-empts the antibody nthe ing mechan m so that the cla ms of the weaker allergen cannot be sati fied The blocking effect la ts about 2 week after appl cation of the nterfering allergen

▶ [These investigations rev al data which strongly suggest the existence of an interference phenomenon. However befor this can be accepted as fact, additional control ill hav to be done As pointed out by Eisen

[1] J Invest. Dermat. 21 163-168, August, 1953

sensitized animal resulting from processes associated with allergic sensitization

There is increasing evidence that the white blood cells in particular the mononuclear cells play an important role in the mechanism of allergic eczematous contact dermatitis. Demonstration of a higher level of radioactivity in the buffy coat of the sensitized guinea pig than in its other blood cells or serum indicates that the cells of the buffy coat carry at least part of the responsible allergen and suggests that they are in some way associated with the allergic process. This finding does not necessarily prove or disprove the presence or absence of an antibody to the responsible allergen

► [No consistent changes in the white blood cell count in sensitized animals were observed during the first 12 hours after challenge. Seeberg (Acta dermat venereol 33 359 1953) had found an increase in the number of granulocytes in the blood 4-7 hours after challenge with the allergen DNCB. Polak (Arch klin u exper Dermat 201 124, 1955) noted a relative increase in mononuclear cells and a relative decrease in polymorphonuclear cells between the 2d and 3d day after the sensitizing exposure, i e before the animals became hypersensitive —Eds]

Influence of Calmette Guérin Bacillus Infection on Dinitrochlorobenzene (DNCB) Contact Eczema of Guinea Pig is discussed by J R Frey and P Wenk[4] (Basel) According to present day knowledge the changed reactivity of the entire skin after sensitization with DNCB is due to an antibody like principle. The authors found that sensitization of the guinea pig skin with DNCB was potentiated by simultaneous intracutaneous inoculation with Calmette Guérin bacillus if both antigens were given simultaneously and in the same skin area so that they reached the same group of regional lymph nodes. When the antigens were applied to separate skin areas so that each reached a different lymph node group potentiation was absent or minimal

Contact eczema according to current theories depend on the development of specific antibodies and an increase in the antibodies must be assumed as a basis for potentiation. Since the authors observations indicated that this potentiation takes place in the regional lymph nodes it may be assumed that antibodies are produced in these lymph nodes. If the source of antibodies were found to be exclusively some organ situated deeper than the regional lymph nodes potentiation would also take place when the antigens are car

(4) Dermatologica 11 1 4-164 September 1 9

ried to this organ by way of different groups of lymph nodes. The authors had shown before that sen tization does not sub de when the regional lymph nodes are remo ed after sen tization has been established. This would suggest that these lymph nodes are not the only producers of antibodies. Further studies hould reveal the nature of the agent which carried on from the regional lymph nodes centripetally and to determine the organs which, besides the regional lymph nodes produce antibodies and preserve sen itization.

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J Invest. Dermat 31 83-108, August, 1958

and Sulzberger in the discussion to this paper the experimental method used does not rule out a nonimmunologic *phenomenon. Also, the role of the* sites of application of the allergens is difficult to assess at this time. The results of Frey and Wenk (see preceding article) for example, clearly show that if two allergens are applied to sites of application which drain into the same regional lymph nodes, this may have a different effect on the degree and incidence of sensitization as compared with application of two allergens to sites draining into different lymph nodes.—Eds.]

Histopathology of Contact Eczema with Reference to Sweat Retention. D. I. McCallum[6] studied serial sections of 45 biopsy specimens from 24 patients with eczema. The sweat ducts in the dermis and rete mucosum appeared to be



Fig. 5 (left).—Part of sweat duct on right of vesicle and intact ampulla.

Fig. 6 (right).—Break in lower layers of stratum corneum around which leukocytes are bound. Stratum corneum in this area shows parakeratosis. Sectioned sweat duct is at base of vesicle on right, and superficial part is extension of spherical vesicle into adjacent midepidermis.

(Courtesy of McCallum, D. I.: T. St. John Hosp. Dermat. Soc., pp. 3-8, Winter 1957.)

resistant to the stresses caused by the eczema reaction. They were usually displaced to one side of the vesicle (Figs. 5 and 6). In a few instances they penetrated the vesicle without rupture. In acute or long standing reactions they appeared to be elongated and compressed between the closely packed vesicles.

At the greatest diameter of the vesicle the layer of stratum corneum lying immediately above the rete mucosum was frequently ruptured and its free margins were inverted into

(6) T. St. John Hosp. Dermat. Soc., pp. 3-8, Winter 1957.

the vesicle cavity The rupture of the stratum corneum occurred at or close to the po nt at which the sweat duct entered the stratum corneum and was close to the ampulla of the duct (F g 6) Frequent rupture of the sweat duct at the lower level of the stratum corneum in acute conditions could explain the sweat retention in some of these cases. It would also explain the deleterious effect of sweating in these condi tio s. When eczema vesiculation is severe enough to rupture the lower layers of the stratum corneum in the vicin ty of the mpulla of the sweat duct stimulation of the gland ould cause extravasation of its secretion into the tissues.

In acute contact eczema degeneration of the epidermal cells of hair follicles was observed, with lymphocytic infiltration around a d within the follicle The infiltration was most pronounced in the upper ep dermis, just under the stratum corneum. In some cases eczema vesicles occurred in the hair follicle. The findings suggest that in cases of contact eczema the allergen gains entry into the skin by the skin appendages. In both epidermis and dermis th s produces hanges wh ch ultimately result in vesiculation. The changes in the epidermis are essentially destructive those in the dermis are exudati e.

► [These findings in contact dermatitis are quite similar to those described in dyshidrotic and esicular eruptions of the palms and soles by Herrmann *et al* (this YEAR BOOK p 227) —Eds]

Subungual Hemorrhage in Pan Washers Preliminary Report. Peter I Long Jr (Dayton, O) reports 3 cases of subu gual hemorrhage in pan washers at the Veterans Ad mini tration Center The 3 patients used heavy rubber gloves while working Other pan washers wore no gloves or only light cotton gloves to protect the hands from steel wool During the interval between discovery of the first and th rd patient the type of cleansing agent used for washing pan was changed from a powdered to a liquid detergent. During the washing process each patient accumulated 50-175 cc washing solution in the rubber gloves. The pH of the solution in th nks was 7 1 10 0 whereas that n the glo es was 5.2-6.7

Only men who had been pan washers for a short time had subungual hemorrhages The fact that they were not accustomed to this type of labor may be an important factor in the cause. However it is unlikely that the lesions were due to

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and Sulzberger in the discussion to this paper the experimental method used does not rule out a nonimmunologic phenomenon. Also, the role of the sites of application of the allergens is difficult to assess at this time. The results of Frey and Wenk (see preceding article) for example, clearly show that if two allergens are applied to sites of application which drain into the same regional lymph nodes, this may have a different effect on the degree and incidence of sensitization as compared with application of the allergens to sites draining into different lymph nodes.—Ed.]

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(6) T. St. John Hosp. Dermat. Soc., pp. 5-8, Winter 1957.

rat of 3.3 4 was obtained for small plants in the chemical and allied products industry This was the highest rate in any size group in any industry category Little seasonal variation in incidence of dermatitis was observed during the 6 months of the study Of 173 cases of dermatitis presumably due to petroleum products, 119 (69%) were considered to be due to cutting oils. Incidence of dermatitis due to cutting oils was 0 22% for all workers and 0.32% for production workers.

The authors con lude that with about 16,000,000 employees in the manufacturing industries it might be expected on the basis of these figures that 128,000 occupational dermatitis cases would occur in the course of a year throughout the country About 60,000 of these would be due to petroleum products, cutting compounds accounting for about 41,000.

Dermatitis Report on 5½-Year Experience of an Ammunition Plant is presented by Arthur L. Knight (Rochester N Y) During the survey period there was a steady drop in the dermatitis rate from 75 cases/1,000,000 man-hours in 1951 t 17 cases n 1937 The yearly occupational dermatitis at dropped from 49 to 8 cases/1,000,000 man hours. The decline in dermatitis was similar to the decline in over-all occupational sickness and accident rate Knight discusses factors bel eved to be important n the reduct on of the occupational disease rate

The tandards f pre-employment examination were raised during the survey period. Employees with a history of dermatitis were not h red for toxic operations. Those with a hi tory f hay fever or a thma were estricted from working n most toxic areas. The physical examination was broadened to includ a omplete kin survey No one with an active skin lesion, such as acne, eczema, dermatophytos s or psoriasis, was hired for work n manufacturing area. Annual examinations, including skin surveys were carried out If a skin disease was detected th employee was kept from to c exposure and w t eated Employees in toxic areas were given monthly medical exam nations. These helped insure that dermatitis did not go undetected and untreated Employees re constantly asked to seek early treatment of kin eruption An effort wa made not to overtreat any dermatitis.

A M A Arch Indust Health [illegible] 47 August, [illegible]

pure trauma because they probably would be more common if this were the case. The change to the acid side in the pH of the detergent solution trapped in the gloves may have caused breakdown of the detergent, with subsequent release of a more irritating substance in the form of a sulfonic acid. This possibility is being investigated.

In the 3 patients subungual hemorrhages subsided and the lesions completely cleared after the patients were removed from their jobs. Prompt recognition of the lesions and elimination of the offending agent is necessary to prevent extensive nail bed damage.

► [The illustrations in this article demonstrate that these subungual hemorrhages are much more massive than the characteristic splinter-like hemorrhages seen associated with subacute bacterial endocarditis and trichinosis.—Eds.]

Dermatitis in Industry: Pilot Study with Special Reference to Oils as Causative Factor is reported by Daniel C. Braun and Rosedith Sitgreaves (Industrial Hygiene Found., Pittsburgh). Records were obtained of every patient with dermatitis reporting to the dispensaries of 36 companies with 103,586 employees. The companies were located in 5 geographic areas and represented 8 industrial categories. The study was carried out during 6 months. There were fewer than 500 employees in 13 companies, 500-1,000 in 7, 1,000-10,000 in 13, 10,000-20,000 in 2 and over 20,000 in 1. Two thirds of all employees covered were in the fabricated metal products industry. All but 1 plant provided exposure to solvents, all but 2 to greases, all but 4 to cutting oils and to chemicals such as acids and alkalis, and all provided some possibility of contact with petroleum products.

For all employees the rate for occupational dermatitis was 0.8% adjusted on an annual basis. The rate for dermatitis due or probably due to oil was 0.3%. When the reported cases were related to production workers only, who were in effect the exposed group, the incidence rose to 1.2% for occupational dermatitis and to 0.5% for dermatitis due to oils and greases. The rates for female production workers were roughly twice the corresponding rates for males. Incidence rates could not be correlated with race and complexion in this study. In general, plants with less than 1,000 employees reported few cases of occupational dermatitis. However a

(8) A.M.A. Arch. Indust. Health 17: 259-272, April, 1958

soiled hands or on the inner thighs due to clenching the shoes between them.

The cement is composed of (1) synthetic rubber Neoprene AC (2) phenolformaldehyde resin CKR 1634 (Union Carbide) composed of para tertiary butylphenol formaldehyde and an unknown catalyst and (3) zinc and magnesium oxides, toluene ethylacetate and benzene. Ten patients patch tested with these substances had reactions to the resin and to para-tertiary butylphenol Two also had reactions to formaldehyde.

Several other commonly used shoe adhesives contain para tertiary butylphenol (or a closely related substance) Several patients sensitized to Saba Select have had recurrences of dermatitis when working with other adhesives

The author proposes several preventive measures All gluing should be done in a separate part of the shop and at a particular time during the day Gloves, aprons and tools should be used only for this work. The soles to be brushed should be held with a fork in slots in the work bench A glove should be worn on the right hand while brushing on the glue and on the left hand while the sole is held in place during hammering The working surface should be covered with a sheet of paper which is discarded at the close of work. Splashes of adhesive on the skin should be removed with ethyl acetate followed by soap and water

► [It would be surprising if allergic contact dermatitis did not occur occasionally in wearers of shoes made with adhesives containing para-tertiary butylphenol —Eds]

Problem of Prolonged and Recurrent Industrial Dermatitis is evaluated by the Committee on Occupational Dermatoses Council on Industrial Health, American Medical Association. The chief reasons for failure to bring about cure in some patients suspected of having occupational dermatoses are listed in the order of their importance.

1 Incorrect dermatologic diagnosis. Such diseases as nummular eczema, infectious eczematoid dermatitis dyshidrosis, superficial fungous infection, lichen planus and psoriasis are frequently misdiagnosed as occupational. A carefully detailed history is most important in establishing a diagnosis of occupational contact dermatitis. Patch tests may be valuable diagnostic aids, but only if used properly

(3) J A M A. 148 314-320, Oct 4, 1952.

Lectures posters and safety talks were used in the direct education of employees

A campaign was undertaken to supply adequate rest rooms of high standard. Each rest room was inspected every 24 weeks A high standard of cleanliness and housekeeping in work areas was developed. Complete change of clothing was furnished daily to workers in toxic areas. Other workers on dirty jobs were furnished coveralls Most employees were given the facilities and opportunity for showering after work Indicator soap was used in TNT toxic areas Investigation and control of dust, fumes solvents gases noise, heat, humidity and nuisances became routine. If possible the environment was controlled and toxic contamination eliminated so that protective equipment could be discontinued. Consequently during the survey period all but two respirators were removed. Fewer protective gloves were required. Protective creams were discontinued Automatic machines, conveyor belts drag lines, etc. were gradually introduced to reduce employee exposure to toxic hazards

► [This article points out that careful industrial engineering together with planning for proper habits of cleanliness of the employees and the selection of workers for specific jobs, can indeed lower the incidence of occupational dermatoses as well as other occupational illnesses and accidents However the case history and results of an examination of the skin for dermatoses require careful evaluation so as not to exclude from work individuals whose cutaneous lesions would in no way introduce a hazard to themselves when employed for selected forms of work —Eds]

Occupational Eczema Due to Para Tertiary Butylphenol in Shoe Adhesive. A few months after introduction of a new type of shoe adhesive K E Malten[1] (Leiden The Netherlands) observed several cases of occupational dermatitis The adhesive, Saba Select is used to bind the outer and inner soles The outer sole is held between the fingers of the left hand and the adhesive is applied with a brush in the right hand then it is allowed to dry for 30 minutes The outer sole is placed on the inner and the soles are hammered together The prevailing sites of dermatitis have been the finger tips and finger webs of the left hand the proximal third of the left palm and occasionally the fingers of the right hand and the volar aspects of both wrists. Lesions have also been observed on the face and neck due to direct contact with the

(1) Dermatologica 117 103 107 August 1958

presence of fungous disease and presence of a constitutional skin disease or atopic background.

► [The high incidence of industrial dermatitis together with the continued introduction of new potential allergenic substances increases the need for careful planning and prophylactic measures in industry in the attempt to avoid primary sensitizations as well as cross-sensitizations.—Eds.]

Prognosis in Industrial Dermatitis. F. F. Hellier[3] (Leeds, England) reports the findings in a follow up by means of a questionnaire of 124 working persons who had been examined 4-6 years previously because of industrial dermatitis. Further attacks of dermatitis had been experienced by 95 patients (80% of the men and 67% of the women). Earning capacity had diminished because of the original attack of dermatitis in 73 instances (59%). In persons over age 50 earning capacity was reduced in 68%; in those under 50 earning capacity was lower in 53%. Among patients whose original dermatitis occurred as a result of primary irritants (soap, detergents, friction, sweating, etc.) only 8 of 59 (14%) had no further trouble, whereas of those who had reacted to sensitizing agents 21 of 65 (32%) remained clear.

Only 29 persons (23%) were still in the work they were doing when dermatitis first occurred. Six patients had never been able to return to work of any kind. Of the 29 who did not change work, 22 (76%) had further attacks; of 89 who changed work, 67 (75%) had subsequent dermatitis. Only 7 persons in the whole group were able to continue at their old work without dermatitis. Of these, 4 had made some modification of the conditions of their work (a bath attendant used a different method of cleaning, a joiner avoided glue, a lamp-fitter wore gloves and an engineer used a heavy barrier cream). The other 3 were a baker, an office cleaner and a coal miner about whom no detailed information was available.

The findings suggest that complete immunity from further attacks of dermatitis rarely comes except with a change of working conditions. It seems, therefore, that a worker who is truly sensitized should be *removed* from the offending agent as soon as possible. However, a change of work does not guarantee freedom from trouble, particularly for those reacting to primary irritants.

► [This study reveals several important facts. Among them is that the chances of permanent clearing are more than twice as great in industrial dermatitis due to allergenic sensitizers than in cases due to primary irri-

(3) Brit. M. J. 1: 196-198, Jan. 23, 1954.

2 Failure to establish cause Discovery of the cause may be especially difficult in workers who go from job to job in the plant

3 *Failure to eliminate the cause after correct discovery and diagnosis* After the skin heals some workers are put back on the same job by supervisory personnel Others are reluctant to give up skilled jobs for those with less pay and continue working with hazardous materials despite medical advice *A complete change of job in the same department* sometimes fails because the air tools benches and doorknobs may be contaminated with the chemicals responsible for the dermatitis.

4 Improper medication This may be a home remedy with which the patient experiments or the wrong type prescribed by the physician

5 Development of secondary infections nummular eczema or dyshidrosis When these complications exist, bland therapy usually effective in uncomplicated dermatitis, fails to achieve satisfactory results

6 Poor facilities and improper cleansing agents Patients with occupational dermatitis are prone to exacerbation from the use of poor-grade alkaline soap and organic fat solvent e.g naphtha kerosene and gasoline for cleansing the hand

7 Placing dermatitis-prone persons on hazardous new jobs.

8. Cross sensitivity Patients may develop dermatitis as a result of *exposure to one substance in the plant and have a* recurrence due to contact with a structurally related chemical either on a new job or in nonoccupational pursuits.

9 Development of multiple reactivities The cause of this phenomenon is not known but it must be considered as a possible reason for persistent dermatitis in a patient who has been removed from contact with the specific allergen or irritant.

10 Malingering *This factor is often suspected but is difficult to prove* Rehabilitation and proper job placement with better compensation laws *should do much to prevent* malingering

Other less important factors that may be responsible for failure to bring about cure in individual cases of occupational dermatitis are active foci of infection elsewhere

eczema, having scattered and grouped pruritic vesicles usually with surrounding erythema suggest dermatitis herpetiformis. With formation of eczematoid orbicular lesions there is a similarity to disseminated nummular eczema. At the multiformity stage a clinical parallel to exudative discoid and lichenoid chronic dermatosis is apparent. In the final stages of a classic cycle of generalized autogenous eczema dermatitis exfoliativa or generalized neurodermatitis are suggested by the clinical picture.

Among the 60 patients an allergic or atopic diathesis was noted in a significant number and most related underlying tensions and emotional difficulties. Such findings are common in the dermatoses which generalized autogenous eczema resembles. Differentiation of these diseases from generalized autogenous eczema rests mainly on the precipitating local dermatitis and close observation of the course of the eruption.

A simple cellular focal vascular reaction was observed in most microscopic sections of generalized autogenous eczema studied and appeared closely related to the neurodermatitic reaction. Complicating secondary histologic features may be present depending on the biopsy site, age of the lesion examined and exogenous factors such as secondary infection, rubbing and scratching and local medication.

These observations suggest that neurodermatitis, nummular eczema, exudative discoid and lichenoid chronic dermatosis, dermatitis herpetiformis and generalized autogenous eczema belong to the same group of diseases.

► [In the experimental animal it has not been possible to engender sensitization to autologous skin using the same technics which did succeed in producing sensitization to autologous brain, testicular and lens substance, etc. (see the following article). Since the basic principle of autosensitization to skin is not as yet firmly formulated, it seems unwise to attempt to apply this concept in such well-established cutaneous entities as atopic dermatitis, dermatitis herpetiformis, and so forth.—Eds.]

Failure to Sensitize to Autologous Skin is reported by Stanley A. Rosenthal, Rudolf L. Baer and Blanka Hagel[*] (New York Univ. Post-Grad. Med. School and Skin and Cancer Unit).

METHOD.—Emulsions of autologous skin were prepared, using samples of skin removed from clipped and shaved flanks of guinea pigs.

(*) Proc. Soc. Exper. Biol. & Med. 97: 279-281, February, 1958.

tants. This is probably explained by the greater opportunity for strict avoidance of known specific sensitizers than of the ill-defined category of "primary irritants." An incidence of 68% recurrences in allergic industrial dermatitis and of 86% recurrences in primary irritant industrial dermatitis is a rather sad commentary on preventive management of these common eruptions.—Eds.]

Thrombocyte Index after Injection of Staphylococcus Vaccine and Tuberculin in Man. A fall in the thrombocyte index on supply of antigen is a common feature of allergy to foods and medicaments. This phenomenon is also observed within a few minutes of administration of pollen extract in human subjects hypersensitive to pollen. In anaphylactic shock in animals and in eczema types of reactions there is also a thrombocyte fall. Åke Nilzén[4] (Karolinska Hosp., Stockholm) made thrombocyte counts every 15 minutes for 90 minutes after injection of staphylococcus vaccine (about 90 000 000 organisms), staphylococcus toxoid (0.3 ml of 1:10 dilution) and tuberculin (0.003 mg.).

A definite fall of the thrombocytes was observed after subcutaneous administration of staphylococcus vaccine and toxoid in patients who showed a positive skin reaction to the allergen. There was no appreciable difference in the thrombocyte fall for subjects with immediate or delayed response. A fall in thrombocyte count was also observed after injection of tuberculin in patients with positive reactions to skin tests with this material. Though some of the controls (with negative skin reactions to the allergen) displayed a reduction in thrombocyte values, there was a clear correlation between the fall of thrombocytes and the positive skin response. A 20% thrombocyte fall was regarded as significant. Results indicate that the fall may be recorded if samples are taken 30 and 75 minutes after injection of the antigen.

► *[These studies confirm the results of Storck, Holgné and Koller and others. Apparently the fall in thrombocyte count occurs on exposure to the allergen in many different forms of allergic sensitization.—Eds.]*

Dynamics of Autosensitization Dermatitis: Clinical and Microscopic Concept of Autoeczematization on the basis of a study of 60 cases is presented by Alexander W. Young Jr.[5] (St. Luke's Hosp., New York). The usual stages of generalized autogenous eczema are the vesicular, organizing, confluent (spreading), multiform (diffuse) and resolving (generalized). The earlier stages of generalized autogenous

(4) Acta dermat.-venereol. 33:112-121, 1953.
(5) A.M.A. Arch. Dermat. 77:495-502, May 1958.

which begins afte age 30 Although about half the patients with constitutional neurodermatit s form reagins, their eti ologic significance is questionable.

It was found that persons with con titutional neuroderma titis without asthma and without allergic rhinitis form re agins less frequently than do those with asthma or allergic rhinitis.

Stud es in 112 families of patient with constitutional neu rodermatitis and 235 fam lies of patients with bronchial asthma and rhiniti poll nosa ev ealed that the indi idual diseases frequently involve the site which is the commonest for that disease in the family

Phenotypic, Familial-Pathologic Behavior of Atopies (Constitutional Neurodermatitis, Bronchial Asthma, Aller gic Rhinitis) U W Schnyder and W Klunker[4] (Univ Skin Clini Zuri h) reviewed th famil es of 347 unselected pa tients with atopic diseases. There were 112 patients with constitutional neurodermatitis, 8(of whom had also respira tory in lvement, and 235 with bronchial asthma and rh ni tis poll nosa

Among the families of the 112 patients with constitutional neurodermat tis, 41% of the P 1 and P 2 generations on the maternal and paternal side were not affected by asthma, rhi n tis or neurod rmatitis. Of 26 patients with neurodermati tis without asthma or rhinitis, 6 (23%) had ancestors with neurodermatiti only In 2 of the 26 families *neurodermatitis* was found on one side of the family and asthma or rh nitis on th other s de

Among the 86 patients with neurodermatitis who also had respiratory affections, if a hereditary trait was present, the ancestors had alternating o n combination manifestations of asthma, rh nitis or neurodermatitis (so-called polyphenia)

In abo t a third of the 235 patients with asthma or rhinitis pollinosa, the allergy manifested tself n 3 generations al way nly as asthma or only as allergic rhin tis, while in tw -thirds the igns f asthma or rh nitis appeared in the ancestors either si gly or in combination. In 11 of the 235 families, neurodermatitis was found among the ancestors.

It concl ded that bronchial asthma and allergic rhinitis, on the one ha d, and const tutional neurodermat tis, on the

Hautarzt 1 November 1957

Skin was weighed to the nearest 0.1 Gm. minced with scissors and added to 4 volumes of sterile saline or staphylococcus toxin diluted 1 5 with saline. This crude skin suspension was fragmented in a high-speed homogenizer The resulting skin broth was taken up through a 20- or 21 gauge needle and emulsified in a syringe with 2 volumes of a mixture of Bayol F and Arlacel A containing 1 mg of killed, dried tubercle bacilli/ml The ratio of Bayol F to Arlacel A was either 8½ 1½ or 2 1 Thus each milliliter of skin-adjuvant emulsion contained approximately 67 mg of skin Test animals received injections of their autologous skin emulsion with adjuvants, whereas control animals were given an emulsion of saline or staphylococcus toxin diluted 1 5 with saline, with adjuvants

Eighty nine guinea pigs were given injections intracutaneously intramuscularly or intraperitoneally with autologous skin emulsion and 38 with control emulsion. Animals received autografts 28-64 days after the first injection of skin or control emulsion. There was no significant difference in the percentages of skin autografts accepted and rejected between the animals pretreated with an emulsion of their own skin and control animals Irritancy tests such as scraping and burning the skin did not produce different results in the two groups Thus neither the autograft experiments nor the irritation tests produced evidence indicating that sensitization to autologous skin had taken place after intracutaneous, intramuscular or intraperitoneal injections of autologous skin and adjuvants

Allergic and Familial Background of Atopies i discussed by U W Schnyder[7] (Univ Skin Clinic, Zurich) Constitutional neurodermatitis (Besnier s prurigo atopic dermatitis) together with bronchial asthma and allergic rhinitis, has been considered as an atopic or familial-dispositional allergic disease However atopic allergy has a different etiologic significance in the three diseases

In the various forms of allergic rhiniti sensitization against pollen grasses feathers various animal hairs and other inhalant allergens has primary etiologic significance The clinical signs of allergic rhinitis usually appear within a few minutes after exposure Of the various forms of bronchial asthma only hay fever and baker s asthma behave as does allergic rhinitis In about 40% of all asthmatics no atopic hypersensitivity can be demonstrated This holds especially for patients with so-called intrinsic a thma"

(7) Dermatologica 116:283 286, April M 1958

onset of hay fever and asthma direct hypnotic suggestions were made for the first time about her symptoms. She was told that she would have no hay fever or asthma. During the ensuing season she was entirely well for the first time. Weekly hypnotic treatment was continued during this period, and she was skin tested on the left arm after each treatment Sensitivity reactions gradually decreased to zero during 7 weeks. However when she was unexpectedly tested on the left leg (a site not previously used for testing) skin tests were again markedly positive. She was then told, while in hypnotic trance, that the skin would henceforth be unresponsive on all parts of her body After this trance skin tests were negative on both arms and both legs. With the patient consistently free from asthma, hay fever and any skin responses when tested with known allergens, a passive transfer test wa performed, and a reaction was obtained w th 2 of the 3 known al lergens.

By direct suggestion under hypnosis an overriding psychic ystem of control was established in this patient, which could not only keep her well but could inhibit selectively the aller gi reaction n different parts of the body Although presum ably central m origin, this control system, because of ts powers of selectivity might be assumed to act peripherally

In this case laboratory control produced results which support the general clinical observation that three factors may be i l ed in the etiology of a thma and hay fever foreign proteins, sensitized tissues and a psychogenic factor In this patient, at least, the psychogenic element was shown to be the most powerful possibly explaining why psychologic treatme t in the form of suggestion under hypnosis provided complete relief from symptoms, whereas other methods of treatment wer only partly successful.

► [A most interesting report of the power of strong hypnotic suggestion on disease and on the reactivity of the skin to urticariogenic allergens. The authors conclusions that the psychogenic element was the most powerful etiologic factor in their patient because of her favorable response to hypnotic suggestion seems unwarranted Would they have concluded that the adrenal glands are the most important etiologic factor if they had suppressed the hay fever and asthma in this patient by giving large doses of corticosteroids or if they had suppressed the skin test reactions to the grasses, trees and spring flowers by the prior administration of epinephrine? —Eds]

Observations on Delayed Blanch Phenomenon in Atopic Subjects. Michael J Davis and James C. Lawler[8] (Walter Reed Army Med. Center) studied the superficial vascular esponse of 15 atopic subjects to locally ppl ed acetylcholine by direct observation of the essels with a capillary mi

[8] J Invest. Dermat. 30 127-131, March, 1958

other do not behave similarly in their phenotype Patients with neurodermatitis without involvement of the respiratory tract usually carry only the hereditary trait of neurodermatitis Neurodermatitis patients with conditions of the respiratory tract usually come from families with manifestations of asthma rhinitis or neurodermatitis. So-called polyphenotypic ancestral lines are rare among patients with atopic diseases They are mostly found among patients with constitutional neurodermatitis and asthma and/or rhinitis.

Pulmonary Function in Endogenous Eczema. According to E Lutz and G W Korting[9] (Univ Skin Clinic, Tubingen) the concomitant as well as the alternating behavior of endogenous eczema and bronchial asthma point to the existence of a *similar* diathesis in both The authors studied pulmonary function (respiratory rate, vital capacity respiratory volume per minute, etc) in 25 patients with endogenous eczema and in 20 controls of about the same age and with similarly extensive skin affections of various cause before and after use of Aludrine an antiasthmatic compound. Latent susceptibility for asthma (pulmonary dystonia) was found in 60% of the patients and in 5% of the controls.

In 8 of 12 patients who had endogenous eczema but no individual or familial asthmatic trait the pulmonary function studies did not reveal pulmonary dystonia. This suggests hereditary familial differences in patients with endogenous eczema, implying that there are families with endogenous eczema with or without involvement of the respiratory tract.

► [These findings fit in with those of Schnyder (see 2 preceding articles) that there are two distinct groups of atopic dermatitis patients, namely those with a hereditary trait for atopic dermatitis and those with a hereditary trait for atopic dermatitis *and* respiratory allergies.—Eds.]

Allergic Skin Responses Abolished under Treatment of Asthma and Hay Fever by Hypnosis A A Mason and Stephen Black[1] (*London*) report a case

Woman, 27 had had incapacitating hay fever and asthma from May to July each year for 1 years. One year previously she had some relief from symptoms after hyposensitization but remained sensitive to 3 known allergens (extracts of grasses trees and spring flowers) Because of the limited benefit obtained from hyposensitization, she refused further treatment of this kind and was referred for hypnosis.

Before the expected onset of symptoms in May she was given weekly hypnotic treatments for 2 months. One week before the expected

(9) Arch. klin. exper Dermat. 205 597-604, 1958
(1) Lancet 1 877-880, Apr 26, 1958.

and Charles F Code[3] (Mayo Clinic and Found.) White dermographi m is the asoconstriction of minute cutaneous vessels and is seen after light stroking of normal skin The reaction persisted w th both light and heavy stroking in chronic inflammation of the skin. The reaction occurred in chronic in filtrati e conditions such as atopic dermatitis d sseminated neurodermatitis psoriatic erythroderma, mycosis fungoides and lymphomatou erythroderma and was not specific for atopic dermatitis. The wh te reaction was not seen in acute nflammatory conditions. Patients with superficial dermatoses such as parapsoriasis pityriasis rosea and superficial localized psoriasis eithe did not exhib t the reaction or showed it only slightly These patients had a red line with a flare or a whit halo Several patients with atopic dermatitis or generalized psoriasis showed loss of white dermographism when the cutaneous lesions disappeared.

In ttempting to inhibit the white reaction, various agents were injected that are known to block the action of chemicals that occur nat rally in the skin and cause vascular responses Diphenhydrami e (Benadryl) hydrochloride was used to inhibit the action of histamine phentolamine (Regitine) hydrochloride to nh bit the action of adrenergic compounds a d atropine to inh bit chol nergic c mpound procaine wa used to produce localized anesthesia. None of these agents jected intradermally inhibited the appearance of the white eaction prod ced by troking

The results seem to imply that white dermographism depend on mechanical timulation of the skin which induces capillary constriction and pparently is independent of any chemical o ners stimulus. In chron c nflammation the ski pillar es pparently are altered by the inflammatory process, and increased ascular tone results.

* [The esults probably showed increased vascular tone as a esult of hronic inflammation Alterations in vascular tone may well be the result of some locally altered biochemistry The question remains whether chronically inflamed skin produces chemical substance as yet unidentified hich is activated to cause asoconstriction following mechanical stimulation of the skin in the diseases noted —Eds]

II *A tion of* *r nephrine and phentolamine* (*egitine*[*]) *ct on* *f acetylcholine and methachol ne* (*mecholyl*[*]) *and delayed blanch* were estigated by Reed and Kierland Epi

3 A.M.A. Arch Derma 77 96, January 958
Ibid pp. 18 186, anuary 1958

croscope The sites were prepared by repeated applications of cellulose tape until the keratin layer had been removed At least 1 hour was then allowed to elapse before testing

Capillaries in the areas of the acetylcholine-induced wheal and delayed blanch reaction remained dilated, though the areas turned pale grossly There was increased accumulation of fluid in the wheal and about its periphery which accounted for the gross paleness The local vasodilating effect of acetylcholine induces a temporary increase in capillary permeability in and about the wheal with consequent leakage of fluid into the corium The fluid leaking out of the capillaries to form a wheal displaces peripherally the tissue fluids present in the area Since there is edema in the corium in atopic dermatitis more fluid is present to be displaced in wheal formation. This could partially explain the pale halo which is noticeable about acetylcholine induced wheals in atopic skin.

The presence of white pseudopods around the periphery of an acetylcholine wheal probably represents the effect of the agent which is being transported through lymphatics away from the injection site and is diffused out of the lymphatics to act on the blood vessels along them

Hyaluronidase diminished the size of the wheal and its paleness when introduced into the skin with or before acetylcholine and the delayed blanch phenomenon did not occur presumably because the fluid was diffused more rapidly

The delay in appearance of a pale zone around the acetylcholine wheal is consistent with the impression that displacement of fluid is involved in formation of the delayed blanch zone. Sweat retention may also contribute to the observed paleness in and about the wheal from acetylcholine possibly by causing maceration of the keratin layer

► [The exact nature of white dermographism and delayed blanch phenomenon in atopic dermatitis remains to be elucidated The findings of Da and Lawler demonstrating vasodilatation and pericapillary edema formation contradict the generally held concept that these phenomena are due to vasoconstriction. The speed with which the blanching occurs in white dermographism perhaps would be explained more readily by vasoconstriction than by edema formation Furthermore if edema formation were the correct explanation one would expect that, occasionally at least, whealing or some other expression of edema would become clinically evident —Eds]

Vascular Reactions in Chronically Inflamed Skin.—*Mechanical stimuli to skin inhibition of white dermographism* was attempted by William B Reed Robert R Kierland

tory processes, the flare being masked partly or completely by the already dilated minute vessels of the skin.

Injection of 48-80 into normal skin produced a strong flare. Inflammation of the skin reduced the size of the flare; the reduction paralleled the acuteness of the cutaneous disease. The size of the wheal also was reduced in more inflammatory conditions; the reduction was more pronounced with 48-80 than with histamine. The weaker response to 48-80 may have resulted from two factors. (1) The histamine released was removed almost immediately by the increased circulation in the skin. (2) The amount of bound histamine available was reduced, with less histamine being liberated by 48-80.

The flare after an injection of histamine in patients with white dermographism can be reduced or abolished when the affected skin is rubbed before or after the injection. Histamine-induced pruritus may be reduced by stroking the skin and thus abolishing the flare response by producing vasoconstriction of the minute vessels of the skin. With release of constriction, pruritus returns.

Monoethanolamine nicotinate, an ester of nicotinic acid that has nicotinic acid activity, did not have the paradoxical action of acetylcholine, viz. production of the delayed blanch, when injected intradermally.

► [Reed and co-workers here have answered a question which many have asked, namely: Is white dermographism specific for atopic dermatitis? While it is most commonly seen in atopic dermatitis, it obviously also occurs in other chronic inflammatory conditions.

The fact that none of the pharmacologic agents tested inhibited white dermographism might be explained by the fact that they do not interfere with direct mechanical stimulation of the capillaries or, as proposed by Davis, that white dermographism is not due to vasoconstriction. However, diphenhydramine, which decreases capillary permeability in addition to blocking certain vascular responses, would have been expected to interfere with white dermographism if Davis' theory is correct.

Thus, white dermographism cannot be used as a pathognomonic sign for atopic dermatitis; the delayed blanch response, described by Lobitz and Campbell, apparently occurs only in atopic dermatitis and only in the affected areas.—Eds.]

Basophil Leukocytes in Urticaria, Asthma and Atopic Dermatitis. Basophil leukocytes and tissue mast cells have several characteristics in common. Both stain metachromatically with basic aniline dyes, contain heparin or a heparin-like substance, and have a high content of histamine. When

nephrine (0 1 ml. of 1 10 000 and 1 100 000 dilutions) was injected into the skin of 11 patients with atopic dermatitis 4 with disseminated neurodermatitis 5 with psoriatic erythroderma and 3 with mycosis fungoides. All patients showed immediate vasoconstriction after epinephrine injection though the size of the blanched zone was smaller in patients with more acute forms of dermatitis.

Phentolamine injected intradermally produced a small red injection wheal with an axon reflex no different from that following injection of isotonic saline solution When both phentolamine and epinephrine were injected intradermally the central portion of the injection wheal was red and was surrounded by a blanched zone produced by the epinephrine The red zone representing the antiadrenergic action of phentolamine slowly expanded engulfing the blanched portion. A dose of 0 1 ml. of 1 1000 phentolamine inhibited completely the effect of 0 1 ml. of 1 10 000 epinephrine

The delayed blanch noted after intradermal injection of acetylcholine in atopic dermatitis was not found in the other inflammatory conditions studied nor was it present in older subjects with disseminated neurodermatitis. This paradoxical reaction to acetylcholine did not occur in zones of normal skin in patients with atopic dermatitis The delayed blanch was inhibited in part or completely by intradermal injection of atropine but not by injection of phentolamine diphenhydramine or procaine This reaction to acetylcholine and other cholinergic drugs when present, may be used to differentiate atopic dermatitis from similar inflammatory cutaneous diseases.

III Action of histamine histamine releaser 48-80 and monoethanolamine nicotinate (nicamin®) were also studied by Reed, Kierland and Code.[5] Histamine (1 10 000 and 1 100 000) and the compound 48-80 (1 100,000 and 1 500,000) a potent histamine releaser were injected into normal skin and into the inflamed skin of patients with atopic dermatitis, disseminated neurodermatitis psoriatic erythroderma and mycosis fungoides The size of the wheal produced by histamine was reduced in more acute conditions but was nearer normal in chronically inflamed and slightly erythematous skin The size of the flare also was reduced in more acutely inflamma

(5) A.M.A. Arch. Derm. 77 263-268 March 1958

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histamine is liberated from mast cells in experimental animals the animals may exhibit symptoms of anaphylactic shock. Because of these findings Hans Rorsman[6] (Univ of Lund) studied the mast cells in the blood of persons with allergic disorders

Using a modification of the method of Moore and James basophil leukocytes were counted in 96 control, 22 patient with urticaria, 20 with asthma and 30 with atopic dermatitis A marked decrease in the number of basophils was found in most cases of urticaria and in some cases a complete disappearance of these cells A few patients had normal count The average count in the control group was 44.8 ± 2.4 cells/cu mm and in cases of urticaria the average count was 8.1 ±2.7 The average for asthmatic was 55.3 ±5.6 cell /cu. mm blood and in atopic dermatitis 44 3 ± 4 6

The decrease in basophils in urticaria is probably the morphologic basis for the decrease in blood histamine that has been observed in this condition. The author found a good correlation between the low histamine content in the blood of certain patients with urticaria and a low basophil count. In patients with higher counts a greater concentration of histamine was found. In 3 patients with cold urticaria a normal basophil count and normal histamine concentration were observed

The factors which determine whether a patient with urticaria has a normal or low basophil count have not been discovered A normal count has been noted in dermographism and emotional urticaria as well as cold urticaria In 3 patients with urticaria pigmentosa the basophil counts were 19.5 15 and 21 5 cells/cu mm respectively whereas in a fourth patient who was allergic to acetylsalicylic acid the count was 2

The basophil count usually returns to normal during the first few days after an acute attack of urticaria but in some cases counts remain low for several week The mechanism causing a decrease in the basophil count in urticaria is not known Possibly the basophil leukocytes are destroyed in the blood stream or migrate into the reacting skin area

► [Robert Bernard, at the *New York Skin and Cancer Unit*, has been able to confirm Rorsman's results in urticaria and atopic dermatitis. — Ed.]

(6) Acta allergol. 12:205-208, 1958.

found lower basophil counts than Rorsman, although the number of atopic dermatitis patients studied thus far is too small to make these differences statistically significant. The results in atopic dermatitis also may depend on the severity and extent of cutaneous involvement. In allergic contact dermatitis Bernard encountered normal basophil counts.—Eds.]

Results of Correlative Statistics in Over 2,000 Electrophoretic Determinations (According to Antweiler) in Neurodermitis Brocq (Atopic Eczema) and Other Eczemas are summarized by C. M. Hasselmann[7] (Univ. of Erlangen). Neurodermitis Brocq is characterized by a papular, shiny, infiltrated, coarsely patterned skin by chronic, intermittent course with severe itching, occasional lymphadenitis and frequent secondary pyoderma, and by its typical localization in the elbows, bends of the knees, neck, forehead, around the eyebrows, sacrum, perianal region, vulva and scrotum.

To detect possible, permanent biochemical changes characteristic of neurodermitis, electrophoretic determinations were carried out on the serum of patients with neurodermitis and various forms of eczema. The Antweiler method was used, which proved to be more dependable and accurate than paper electrophoresis.

As normal mean values, those suggested by Wernsdorfer were considered: albumin 58.8 ± 1.7, alpha globulin 9.4 ± 0.6, beta globulin 11.6 ± 0.6, gamma globulin 19.4 ± 0.4.

Using the statistical formula

$$\frac{(\bar{X}_{a} - \bar{X}_{b})}{\sqrt{\frac{\sigma^{2}}{N} + \frac{\sigma^{2}}{N}}}$$

neurodermitis patients showed significantly decreased albumin, significantly *increased* gamma globulin and questionably increased beta globulin. Similarly, hypoalbuminemia and increased beta and gamma globulins were found in two groups of eczematous patients. Significantly increased alpha globulin were found in one group of eczematous patients.

The highest alpha globulin reading (24.4%) was found in a woman with psoriatic erythroderma and the highest beta globulin (34.2%) in a woman with latent syphilis and hepatitis. The highest gamma globulin reading of 61.3% was seen in a man with chronic eczema and of 61.7% in a woman

(7) Arch. klin. u. exper. Dermat. 203:373-380, 1957.

with icterus during treatment for malaria. The lowest albumin reading 21.2% was seen in a man with pemphigus.

The combination of increased beta and gamma globulin is interpreted as the typical "plasma syndrome" of a diseased liver. The apparent practical insignificance of these findings together with the obscurity surrounding the etiology of neurodermitis combined with the almost "demonic" recurrences and clinical course suggest correlation of the clinical appearance of the disease with the psychosomatic make-up of the patient.

► [The wealth of significant findings regarding atopic dermatitis which have been accumulated weighs heavily against the apparent practical insignificance of these electrophoretic findings. While no *single* etiologic mechanism has been found (and while perhaps none exists) the knowledge available on atopic dermatitis surpasses that available for certain other common dermatoses (e.g., psoriasis, lichen planus) by far. The "demonic" recurrences of atopic dermatitis generally are readily amenable to treatment and when successfully treated appear to leave a patient with no more than the average amount of emotional problems.

It is of interest, in view of Hasselmann's electrophoretic observations, that Robert Good has reported that atopic dermatitis does occur among subjects with agammaglobulinemia.—Eds.]

Cholinergic Urticaria and Miliaria. Maurice Garrett (Univ. College Hosp., London) studied 2 cases of typical cholinergic urticaria. The patients were young men who described attacks of small irritating wheals which occurred at embarrassing interviews, at dances or when playing football. Hot weather always made the disease worse. Whealing could be produced in both patients by warming the arm in water at 45 C. for 20 minutes, by an injection of pilocarpine or by exercise on a stationary bicycle. One patient stated that he could not sweat and that the rash appeared when he was hot. In both patients during whealing produced by heating copious sweating occurred from the axillae, neck, face, groins and feet, but only a little sweating on the trunk and thighs where lesions were most profuse. The wheals consisted of papules 2-3 mm. in diameter, dome shaped and pale pink, and around them an intense flare spread over an area about 4 cm. in diameter. There were no pseudopodia.

Lesions were produced experimentally by heating the arm in water at 45 C. and were excised as biopsy specimens. In the first case 1 sweat duct showed intercellular edema and

(8) Brit. J. Dermat. 70:166-170, May, 1958.

partial disruption of the lining cells in the superficial part of the duct at the point where it passed into the epidermis. There was some fluid exudation into the dermis at this site. Although the duct opening showed a keratotic ring no proof f pore closure could be demonstrated in serial sections. In the second case the sweat duct was tortuous and the lining cells at the superficial end were separated by edema. There was a vesicle in the epidermis n close apposition to the sweat duct There was no evidence of po e closure.

The findings suggest that the lesion that has been called cholinergic urticaria is not primarily a dermal edema, but is a spongiotic epidermal lesion having many features in com mon with the changes described in prickly heat. Lesions resembling urticarial wheals could conceivably occur in cholinergic urticaria if exudation of sweat from a disordered sweat duct took place mainly from the subepidermal part of the duct. The increased whealing under collodion noted by Grant and co-workers in this condition would be expected if the disease were analogous to prickly heat, which is accentuated by maceration and by adherent substances such as adhesive plaster and collodion. Further the small pale papule surrounded by a large flar seen n these cases is not typical of histamine urticaria.

Lanolin has been recommended for use in miliaria on the ground that softeni g the keratin plugs will allow free drainage of sweat d cts. These 2 patients were not benefited by lanolin applications, but after mild exfoliating doses of ul traviolet light twice weekly for 2 months they were free from urt carial lesions fo 20 and 6 months, respectively

► [The ell-know evanescent lesions of cholinergic urticaria could hardly be explained as process taking place in the epidermis. Spongiosis undoubtedly requires much more time to develop and to disappear than it takes for the heals of cholinergic urticaria to come and go

There is no question that sweat does contain urticariogenic agents. Sulzberger et al (J Invest. Dermat. 21 293 1953) found that when sweat ducts ar obstructed while the secreting acini maintain their function, autogenous sweat which is forced into the tissues can produce discomfort, itching and clinical and subclinical wheals. Further, if an epidermal process, as the one described, was esponsible for the wheals, one would expect similar wheals to occur with miliaria—which is not the case.—Eds]

3 DERMATOSES DUE TO PHYSICAL AGENTS

Light Dermatoses. F P Scott and S M C. Molhuysen v d. Walle[9] (Univ of Amsterdam) tested the sensitivity of patients with various light dermatoses to different wavelengths of the solar spectrum Included were 19 patients with dermatitis solaris, 27 with prurigo aestivalis and 18 with chronic discoid lupus erythematosus. The following skin reactions and methods to evoke them were used to estimate sensitivity (1) For sunburn erythema, caused by wavelengths of 297 302 mμ a monochromator was used. (2) For direct pigmentation caused by near ultraviolet rays of 320–460 mμ, a Philips sun lamp was used for 10 minutes at 30 cm a sunburn reaction was prevented by inserting a 1 mm thick glass slide between the lamp and irradiated skin (3) For direct erythema, caused by heat and infrared rays a Philips sun lamp (ultraviolet and infrared) was used for 10 minutes at 30 cm with a 1 mm glass slide inserted to prevent sunburn reaction.

The studies showed a difference in sensitivity to erythema producing rays in the three types of light dermatoses investigated Patients with dermatitis solaris were more sensitive to the short sunburn rays than normal persons and also showed more secondary erythema reactions to long rays Patients with prurigo aestivalis showed a diminished reactivity to the sunburn spectrum no deviation of normal reaction to the long direct erythema producing rays could be demonstrated. Patients with chronic discoid lupus erythematosus did not show a sunburn reaction deviating from normal and showed no hypersensitivity to ultraviolet rays a is generally accepted. They did show however an increased sensitivity to the long direct erythema producing rays Rays longer than the sunburn producing ones may be responsible for certain dermatoses without the occurrence of sensitizing substances

► [It is possible that various parts of the light spectrum may cause dermatoses without the occurrence of sensitizing substances However t i not clear to us how the tests reported in th rticle prove thi The finding of *diminished* sensitivity to the sunburn part f the spectrum patient with prurigo aestivalis is contrary to the eport of other investigators (Epstein, S J Invest Dermat. 5 187 1942) —Eds]

(9) Dermatologica 116 96-104 1958

Photoallergy and Photocross Sensitivity to Phenergan occurred n a patient observed by Stephan Epstein and Rich ard J Rowe[1] (Marshfield Wis., Clinic) The patient had a dermatitis due to Phenergan sensitivity and photosensitivi ty superimposed on a dermatitis of unknown origin. The photosensitivity was induced by oral administration of the drug at no time had the patient used Phenergan externally A short period of el mination of Phenergan* during the early stage was follow ed by improvement and resumption of the drug by aggravation. Patch tests and photo patch tests demonstrated that the patient apparently was contact sensi tive to Phenergan only but photoallergic to Phenergan and chlorpromazine. Both drugs are phenothiazine deriva t es

I photosensitivity a distinction must be made between phototoxic and photoallergic mechanisms. Phototoxicity refers to those nonallergic phenomena which can be produced at w ll pro ided enough of the drug and proper rays are used. *Photoallergic reactions on the contrary are not normal, obligatory reactions* they occur only in a certain number of persons By no means all perhaps only a few cases of photosensiti ity fr m phenothiazine derivatives, are based on photoallergy

A peculiarity of photoallergy to phenothiazine derivatives is that many patients so affected exhibit a double sensitivity a pla n contact sens tivity against Phenergan or chlorpromazine tself and a photocontact sensitivity to a presumed oxidation o decomposition product of these drugs formed in the skin The photoallergic reaction apparently i an allergic esponse independent of the plain contact sensitivity

Photocross-sensitivity between Phenergan* and chlor promazin ma exist though plain contact sensit vity (without light) can be demonstrated t only one of the drugs. This was hown in this patient who was contact sensit ve to Phenergan only but photoallergic to both drugs.

► [Photoallergy is assuming an increasing importance, probably due to the mounting number of synthetic substances to which are all exposed and the fact that some have photoallergic properties It ll probably be necessary in the future to test new synthetic drugs, contactants, etc not only for their allergenic properties but also for possible photoallergic activity There as photocontact cross-sensitivity but no contact cross-sensiti ity between Phenergan and chlorpromazine in Epstein and Row

[1] J Invest Dermat 29 126, November 957

patient. The most reasonable explanation for this difference in response is that exposure to light resulted in a transformation product from both substances which had contact allergenic properties. This would be in consonance with the simplest and most reasonable hypothesis of the mechanism of photoallergy: light is essential only for release or production of the actual allergen and from there on the reaction proceeds as any other allergic reaction without the necessity for light.—Eds.]

Photoallergic Eczema Due to Blankophores (Optic Brightening Agents) was studied by W. Burckhardt[2] (City Outpatient Clinic for Skin Diseases, Zurich). Many skin diseases affect only the areas exposed to light and are aggravated by light. In some diseases light appears to be the only causative factor. There are exogenous, endogenous and infectious factors which, combined with light, lead to diseases. The blank



Fig. 7.—Photoallergic eczema after use of detergents containing blankophores. (Courtesy of Burckhardt, W.: Hautarzt 8:486-488, November, 1957.)

(2) Hautarzt 8:486-488, November, 1957.

ophores play an important role among the compounds that through external application lead to photoallergic reactions. During the last few years, optic brightening agents have been added to detergents white paper and to textiles to transform the i visible ultraviolet light into visible blue. If the solution of such detergent is viewed under a Wood light, vivid bluish fluorescence becomes apparent. These blanko phore substances are chemically related to the sulfonamides

The author observed 2 patients in whom after use of detergents containing brightening agents eczema developed in light-exposed skin areas, on the face, hands neck and forearms (Fig 7) Restriction of the eczema to light-exposed areas suggested the possibility that the sun rays played an etiologic role The author therefore exposed a skin area that had been pretreated intensively with the detergent solution in question to radiation from a Kromayer lamp filteri g out, however the erythema-producing ultraviolet part of the ra diation. The radiation led to severe ec ematous reactions. The eczema recurred in each patient on re-exposure to th sam detergent. One patient recovered completely but the other had ecurrences of eczema due to light sens tivity

► [Thus far no cases have been reported in the United States of photoallergic eruptions due to blankophores in soaps and detergents. These substances also are called optical bleaches, brighteners, bluening agents and fluorescent bleaches (Villaume, F C J Am Oil Chem. Soc. 35 558, 1958) Many different types of chemical compounds are in use and, according to the best information available to us, it is no longer possible to buy laundry soap or detergent in the United States which does not contain one of these substances This of course does not mean that any of the substances used in this country necessarily are potential causes of photoallergic reactions in man Nevertheless, here is another example of possible harm from the growing number of additives to foods, drugs, contact arts and other materials to which all are exposed daily usually unbeknown to even the best informed among us

Nonfluorescent dyes on cloth reflect part of the visible light which is then perceived as color The nonreflected part is converted into longer (infrared) wavelengths and therefore is radiated as heat The fluorescent dyes on cloth absorb practically no visible light Instead they absorb invisible ultraviolet light and reflect it as visible blue light, thus causing the very white appearance of the cloth —Eds]

Clinical Picture and Differential Diagnosis of Lupus Erythematosus-Like Light Eruptions. According to G Weber[4] (Mainz Germany) lupus erythematosus like light eruption mu t be differentiated from chronic lupus erythematosus. Al though sunlight causes the former it only influences the lat

[4] Hautarzt 9: 408-414, September 1958

ter Light eruption affects only light-exposed areas, especial ly the face, but chronic lupus erythematosus may under certain circumstances involve any area of the body

Sharply circumscribed moderately elevated, round, oval or polycyclic lentil to silver dollar sized carmine red patches which often appear in groups make up the picture of light eruption The smooth surface of the lesions is soon changed by scaling causing them to resemble lupus erythematosu In the latter strong adherence of the scales to the skin pronounced hypersensitivity and atrophic zones, usually starting in the center of the lesions make differentiation from lupus erythematosus like light eruption possible. Subjective symptoms such as burning and itching may be present in both diseases

Histologically light eruption is characterized by mild to moderate hyperkeratosis In one of the author s patients, parakeratosis was also present. Intraepidermal and intracutaneous edema and perivascular mainly lymphocytic infiltrations dominate the picture The dilated blood filled vessels show no proliferation of the intima or media Elastic fibers are preserved in their structure and continuity The subepidermal border zone has normal width bounds and staining properties

Chronic lupus erythematosus is characterized by hyperkeratosis that affects mainly the follicles by atrophy of the epidermis and cutis liquefaction necrosis of the basal cells and lymphocytic infiltration around the skin appendages The collagen fibers are also involved The main differential characteristic is behavior of the PAS reactive subepidermal border zone, which shows considerable widening especially during exacerbation

Therapy consists of light protective ointment nicotinic acid, Atabrine* and chloroquine The last drug appeared to be effective in both chronic lupus erythematosu and lupus eryth [illegible] to Pathogen

Tris [illegible] Venereal Dis esis.

eases, Zurich) investigated the toxic or allergic role of light in the cause of light eruptions Antibodies can be shown only in a few allergic diseases in general Similarly antibodies

(4) Dermatologica 116 223-229 Apr May 1958

would be expected to be found only in some instances of allergic light eruptions. Individual hypersensitivity to rays of the sun or to rays of the sun plus an additional factor has to be proved by various test methods. Light eruptions, classified in the table, may be due to light alone, to combined light and

Pathogenesis of Light Eruptions

Light Alone Effective	Light and Exogenous Factor Effective	Light and Endogenous Factor Effective	Light and Infectious Factor Effective
	Toxic Pathogenesis		
Phototrauma	Photosensitization through plants, dyes, coal tar	Hydroa vacciniforme in congenital, familial porphyria	Photobiotropism
Sunburn			Herpes solaris
Light cancer			Actinic exanthema in lymphogranuloma inguinale
Xeroderma pigmentosum			
Cheilitis solaris			
	Allergic Pathogenesis		
Actinic urticaria	Actinic exanthema due to sulfanilamide phenothiazine	Polymorphonuclear actinic exanthema	
	Para-aminobenzoic acid ester	Allergy to Kimmig substance or to porphyrins	
	Para-aminosalicylic acid		
	Blankophoren		

endo- or exogenous noxious factors or to photobiotropism when light causes exacerbation of a latent infection.

When determining hypersensitivity to light, the various wavelengths must be tested separately. In absence of large spectrographs, filters must be used that are permeable only to certain segments of the spectrum. The erythema-producing wavelength of 2,800-3,150 A alone rarely cause derma

toses. Often there is hypersensitivity only to rays with wavelengths of 3 150-4,000 A. With the latter rays the normal skin can be irradiated for 30-60 minutes, causing only slight reddening and light immediate pigmentation. Nodular or vesicular reaction is pathologic.

► [A useful working classification of the light eruptions. Occasionally it may be difficult to ascertain whether the exogenous pathogenic factor, e.g. sulfanilamide, para-aminobenzoic acid, certain dyes, plants, etc., plays a phototoxic or photoallergenic role.—Eds.]

Sensitivity to Fluorescent (Blue-Green) Light. In most cases of solar erythema previously reported in which light tests have been elicited the action spectrum was below 3,900 A. John H Lamb Phyllis E. Jones Gerbert Rebell and Herman D Alston[1] (Oklahoma City) report 4 cases of erythema perstans type of sensitivity to visible fluorescent light in the range of 4 000-7 000 A.

Schoolteacher white 45 noted redness and burning of the face and neck after several hours driving in a new car which had antiglare, bluish violet pigments incorporated in the windshield. This phenomenon recurred each time she rode in the car The next month she noted burning and redness of the exposed areas of the skin when she walked home from school for lunch. When she returned to school the erythema quickly subsided. However each day the redness and burning lasted a little longer One month later she observed that after her 30-minute toilette in the bathroom she had the same symptoms. White fluorescent bulbs were used in the fixtures on each side of the bathroom mirror She consulted an allergist who made the diagnosis of a blue-light sensitivity He prescribed chloroquine 400 mg once daily and a light screening ointment (A Fil) No appreciable improvement ensued.

When first examined by the authors, th exposed skin on the arms and below the knees showed a deep red erythema. The neck showed poikiloderma like changes, and there was persistent erythema of both cheeks. Exposure of a 3×4 in. area of the back to two 5-watt fluorescent lights (white bulb) at 6 in distance resulted in a faint patchy erythema in 9 minutes. At 15 minutes there was 4+ erythema and [illegible]

[illegible] watt incandescent light with a [illegible] 19 in. from the skin caused an urticarial response Addition of frosted glass failed to decrease the reaction to this more powerful light source Skol[9] (absorption spectrum 2,500-3,200 A) was placed over the skin exposed to both fluorescent and incandescent light It caused no appreciable change in the erythematous reaction

(1) A.M.A Arch. Dermat 77 519-525 May 1958

Therapy consisted of removal of fluorescent light sources and weekly injections of testosterone. After 4 months, the patient's skin became tanned, and all tests to blue light were negati e.

Because of the popularity of fluorescent lighting the der matologist sho ld be cognizant of its photosensitizing action in erythema solare, subacute lupus erythematosus and poly morph c l ght eruptions that fail to clear with antimalarials. These drugs seem to protect patients from the action spec trum approximately t the end of the sunburn spectrum 3,100 to about 3,600 A.

► [In this particular instance and for the sake of clarity it would be better to refer to the action spectrum which elicits the light sensitive eruption rather than the source of the light or the color emitted, as different substances produce fluorescence at different w velengths of light. Of course, Lamb and his collaborators ar referring to sensitivity to light emitted by fluorescent light bulbs rather than fluorescent light.

The increasing interest in photodynamic and photoallergic sensitization gives promise that the very wide gaps in knowledge in this field will gradually be filled. Classification of these eruptions based on the eliciting wave lengths of light and on their morphologic characteristics is only fir t step. However the principal task still remains to ascertain what substance or substances in the skin actually produce the abnormal sensitivity to light. These could be abnormal endogenous metabolites or exogenous substances (as chemically altered or unaltered state) or they could be combination products of exogenous substances with autochthonous products.—Eds.]

Urticaria-Like Reaction after X ray Treatment. G Weber[4] (Univ of Mainz) reports a case.

Man, 69 was gi en -ray treatment for several basal cell epitheliomas on the face and trunk. Dose was 500 r and the factors were 4 cm focus-skin distance, no filter 50 kv and 2 ma. Erythema and urticaria-like lesions appeared in the treated areas 6 hours later. In areas wher treated lesions were close together diffuse, urticaria-like swell ng ppeared, apparently resulting from overlapping of roentgen ray. Tests with arious total dosages of roentgen rays given at 55 kv and with arying kilovoltage but constant *quantity of x-rays* (500) indicated that the urticaria-causing effect of the roentgen rays was more dependent on total dosage than on the voltage-induced wavelength.

Serum of cantharides bl ster of the patient was transferred to control patient and 4 hours later the area was treated with 500 An inflamed urticaria-like eruption developed fter 4 hours on the treat ed site and disappeared within the next 24 hours. A similar eaction resulted when serum from the patient was treated with 500 x rays before being transferred to the control subject. Similar tests with blister serum from normal control ga negative results. Use of sulfhydryl-containing compound (5% cysteine) as protection from the effect of ray did not prevent the urticarial response that resulted when the patient' serum wa used in these experiments.

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[4] J Invest. Dermat 30 1 1 1, June, 1958

These findings demonstrate that the human skin can be sensitized not only to visible light but also to considerably shorter electromagnetic waves (roentgen rays) The presence of an antigen antibody reaction is proved by the passive transfer of the antibodies Roentgen rays do not have the characteristics of an antigen but probably liberate an antigen as evidenced by the results of irradiation of the patient's serum in vitro That the use of a sulfhydryl compound as protection from radiation could not stop the development of the urticaria like eruption is unexplained

► [The patient's urticaria like reaction to roentgen rays is most unusual Some of the results of the immunologic studies reported here are difficult to reconcile with previous findings in the field of hypersensitivity to other physical agents. Passive transfer by the blister fluid technic is not generally considered an acceptable method Previous attempts by other investigators to produce the allergen in vitro by exposure of the patient blood serum to light or cold have failed.—Ed.]

Influence of Varying Physical Factors on Patch Test Responses was studied by William A Anderson Harry Shatin and Orlando Canizares[7] (VA Hosp Bronx, N Y) Patch tests were performed with 5 mm. high wood squares and wood disks with smoothed edges and with similar wood squares and disks with edges rounded off completely Twenty-seven 26 and 25 subjects were tested with 18 mm squares of sponge rubber 5 mm 10 mm and 15 mm high, respectively An appreciable number of reactions resulted where the wood squares and disks with smoothed edges were used but no reactions were observed in a series of 20 tests with wood squares and disks with rounded edges With the 5 mm. rubber squares 25 of the 27 subjects tested showed no reaction 30 minutes after removing the patch No subject showed evidence of reaction after 24 hours. The 10-mm. high rubber squares produced reactions similar to those produced by the wood square or disk both qualitatively and quantitatively with about 35% of subjects showing a reaction after 24 hours. With the 15-mm high squares of rubber the reactions were more marked qualitatively and quantitatively over 50% of the subjects reacting at 24 hours

The nonspecific reactions observed with wood disks and squares and with thick squares of sponge rubber occurred primarily at the margins of the test site The marginal nature of the reaction to wood squares and disks with smoothed

(7) J I vest. Dermat. 40 77-82, February 1958.

edges in contrast to the absence of reaction to the wood disks and squares with rounded edges, indicates that the reactions wer due to the traumatic effect caused by what is basically a cutting edge resulting from pressure. If an elastic substance s ch as sponge rubber is thick enough and sufficiently com p essed, it can also produce a nonspecific traumatic effect.

In performing patch tests with hard substances the poss bility of these nonspecific reactions should be considered Pressure can also potentuate a patch test with an allergen particularly at higher d'lution o in persons with a low degree of sensitivity

► [The incidence of false positive reactions obtained by the author is no indication that any variations in established and time-tested technics of patch testing cannot be made without carefully planned and thorough investigation —Eds]

Occurrence of Urticaria (Erythema) Due to Both Cold and Heat. Urticaria and/or erythema from cold or heat i a w ll known phenomenon. However cases of urticaria or erythema from both cold and heat are rare. George Rajka, Jr and Elizabeth Vmcze[4] report 2 cases

CASE 1 —Man had urticaria during cold weather with a remission in spring but during hot weather the urticaria recurred. Local urti caria resulted from contact with cold running w ter (28 C.) and hot running water (42-44 C) Urticaria also appeared after drinking hot tea, after exposure to heat, psychic stimuli and exercise.

CASE 2 —Man, 24 had patches of erythema on the skin, after contact ith cold air after cold bath and after hurrying and getting hot. The erythema persisted 1 3 hours. Exposure to hot or cold water ice or chlorethyl spray caused erythema but not urticaria. Erythema also occurred fter drinking hot tea, exercise, emotional disturbances and subcutaneous injection of 10 mg pilocarpine.

Some of these findings suggested an allergic mechanism whereas others seemed to indicate a nonallergic cause. The xact pathogenesi has not been determined. In favor of an allergic mechanism the uthors list (1) occurrence of sudden tta ks, (2) positi e dermal and exposure tests, (3) presence of itching nd (4) a efractory phase after positi e tests. Evidence for nonallergi mechanism includes (1) presence of ymptoms after both heat and cold (2) negative passi e transfer (3) dim i bed pathologic esponse during prolonged drug-induced leep, (4) absence of personal and faml h tory of atopy and (5) presence of focal infection.

► [The first case resembles cases described by Hopkins, Kesten and Hazel

4 Acta allergol 3 30 38 1950

(Arch. Dermat. u. Syph. 38:679, 1938). As pointed out by Rajka and Vincze, the question as to whether both the heat and cold urticaria in these cases or only one of these or neither is based on an allergic mechanism cannot be definitely answered at present.—Eds.]

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4 DRUG REACTIONS

Severe Reactions to Antibiotics: Nationwide Survey of hospitals comprising about one third of all general hospital beds in the United States is reported by Henry Welch, C. N. Lewis, H. L. Weinstein and B. B. Boeckman[9] (Food and Drug Admin.). All severe reactions occurring in these hospitals from late 1953 to early 1957 were investigated and classified.

Of available antibiotics, penicillin was found to produce the greatest number and the most severe reactions. Of 1,070 reactions considered to be life threatening, 901 were due to penicillin. Anaphylactoid shock, the most frequent serious reaction to penicillin, resulted in a fatality rate of about 9%. Most reactions to the drug occurred when it was given intramuscularly. No deaths resulted from its oral administration. Of 1,925 reactions classified as not severe or life threatening, 1,616 were due to penicillin.

In order of frequency, the life-threatening reactions to antibiotics were shock, superinfections, severe skin reactions, blood dyscrasias and angioneurotic edema with respiratory tract involvement. The most frequent minor reaction was angioneurotic edema and urticaria. The broad spectrum antibiotics caused relatively few adverse reactions. Tetracyclines accounted for most cases of severe superinfections. Of these, enterocolitis was the most common and most severe. It occurred particularly often in patients undergoing abdominal surgery, and mortality was high. The commonest severe dermal reaction was exfoliative dermatitis, of which 10% of cases were fatal. Erythema multiforme and anaphylactoid purpura accounted for the other severe dermal reactions; 1 case terminated fatally. In the blood dyscrasia group, aplastic anemia was the most common, accounting for 23 of 27 deaths. Blood dyscrasias were most often associated with use of chloram

(9) Antibiotic Med. & Clin. Therap. 4:800-813, December, 1957.

phenicol. Angioneurotic edema with involvement of the respiratory tract was commonly caused by intramuscular injections of penicillin 38 cases were reported, with a fatality rate of 13%

The survey re-emphasizes the need for caution in administering antibiotics. A study of case histories did not reveal indiscriminate use of penicillin by physicians but rather an expected increased incidence of reactions through wide use of a highly antigenic substance.

► [An important and informative article which should be read in the original It is evident that although the over-all incidence of systemic reactions from penicillin is small, considering the number of injections given and tablets taken per year the reactions can be so severe, even including death, that this antibiotic should be considered "potentially dangerous" drug T think of penicillin in this way will not preclude its use but will make the physician review all fact before deciding to administer it by injection

Just as in other categories of drugs, antibiotics must be selected not only for their spectrum of antibiotic effect but also with regard to the undesirable reactions such may occur The physician should be prepared to cope with severe reactions resulting from the antibiotic and the patient as well should be briefed as to what course to follow in the event of undesirable reactions —Eds]

Dermatitis Medicamentosa Due to Diuril® (Chlorothiazide) Report of Three Cases is presented by James R. Rogin (Detroit)

Case 1.—Woman, 37 had a brightly erythematous and papular eruption, with a few scattered papulovesicles on the upper and lower extremities The eruption appeared 8 days after she took chlorothiazide, 250 mg twice daily for 2 days, for premenstrual edema. It was accompanied by much edema of the ankles, lower legs and hands. There was no history of ingestion of other drugs. The eruption persisted 2 weeks, during which time the patient was treated with antihistamines, colloid baths and lotion.

Case —Woman, 6_, was given chlorothiazide, 250 mg twice daily for 10 days, at which time generalized erythematopapular eruption appeared on the trunk and extremities. Ther were also many purpuric lesions The eruption disappeared completely 2 weeks fter chlorothiazide was discontinued, although other medication for cardiac congestion w ontinued during th time.

Case 3.—Woman 42, had taken chlorothiazide irregularly for 6 month or premenstrual edema and tension. During the 6th month, she took 500 mg chlorothiazide once da ly for 8 days. On the 8th day erythematopapular eruption appeared and spread over the upper and lower extremities and neck. The eruption was accompanied by edema of the feet, lower legs and hands. Because of the intense pruritus,

1 A.M.A. Arch Dermat 78 584 1958, October 1958

she was treated with triamcinolone. The eruption disappeared within 1 week but severe pruritus was still present.

► [We have heard also of several cases of photosensitization dermatitis due to Diuril® —Eds.]

Dermatitis Caused by Penicillin in Milk. Since the introduction of machine milking the incidence of mastitis in cows has increased and the common practice among herdsmen is to inject 100 000 units of procaine penicillin into the teat of the infected quarter. As a result of this treatment milk may contain penicillin. If patients previously sensitized to penicillin drink milk containing penicillin dermatitis may develop and persist indefinitely if its true nature is not recognized. H. R. Vickers, L. Bagratuni and Suzanne Alexander[2] (Radcliffe Infirm., Oxford, England) report 2 cases of dermatitis apparently due to penicillin in milk.

CASE 1.—Woman, 55, had had recurrent attacks of dermatitis for 6 years. History revealed several attacks of contact dermatitis due to various allergens including penicillin. She had lived on farms for many years. One year before the present severe attack of dermatitis she had her own cow, which had not been treated with penicillin. During this time she had no recurrences of dermatitis. When her cow stopped lactating she drank fresh bulked milk and had a relapse. Analysis of this milk showed a penicillin content of 4 units/ml. Desensitization to penicillin was carried out, starting with 1 unit intramuscularly. This treatment was continued until she was able to tolerate 1 000,000 units. The dermatitis cleared, and she was able to return to drinking cow's milk without relapse.

CASE 2.—Man, 44, had an acute generalized vesicular dermatitis. He had been treating his cows with penicillin for mastitis off and on for 2 years. He had started to treat 1 cow 10 days previously. Milk from this cow had been added to the rest of the farm milk which he had been drinking. Patch tests were positive for penicillin. The eruption subsided rapidly under treatment with prednisolone.

The American Food and Drug Administration has ruled that milk from any cow treated with penicillin should be discarded for 72 hours. This order, however, is not universally observed and sometimes penicillin may even have been added to milk as a preservative. In Britain there is an indefinite ruling that milk from infected cattle shall not be distributed. Because mastitis can often be diagnosed early and penicillin usually produces a rapid cure, most of the milk from mildly infected cattle is distributed in the normal way. Since the number of persons sensitive to penicillin is increasing with wider use of the drug, the authors feel that

(2) Lancet 1 351-352, Feb. 15, 195[illegible]

th American ruling proh biting distribution of milk for 72 hours after treatment of mastitis hould be adopted in Brit ain

► [Another of the many hidden sources of allergens hich threaten man living in our modern civilization W also observed patient in whom all the evidence, including tests of avoidance and re-exposure, pointed toward fixed urticarial reaction due to penicillin in milk —Eds.]

Sensitivity to Repository Penicillins. R. R. Willcox and G R Fryers[3] (London) present a retrospective study of the side effects observed after administration of 7,300 injection of four repository penicillin penicillin n oil and beeswax, procaine penicillin with aluminum monostearate benzathine penicillin and ben thamine penicillin The injection were given 893 patients during 11 years.

The over-all ncidence of probable reactions was 2.9% of patients nd 0.4% of injections. If all possibl reactions are in cluded, the figures are 4.8 and 0.6% respectiv ly The incidence of reactions was low after single injections but n creased with the number of injections up to 9 after which there was an apparent fall. No reactions were noted with a dosage of less than 1 mega unit, the bulk being found in the 1 19.9 mega unit total dosage range, with a marked fall thereafter by which time most of the sensitivity likely to occur had probably declared itself The incidence of reactions in pa tients known to have had pen cillin previously was 3.6% compared with 2.8 % patients not known to have had previous treatment. Patients with leg ulceration were particu la ly pron to sensiti ty probably because of previous top cal use of penicillin.

There was no significant difference in the incidenc of reactions to the various types of long-acting penicillin and no evidence of unusually prolonged or delayed reactions after the use of repository penicillin. One fatality occurred. Thi was d to bronchopneumonia compl cating dermatiti after penicill n in oil and beeswax. N unequivocal anaphyl cto d reactions were observed

Cutaneous Eruptions after Use of Salk Poliomyelitis Vaccine. Despite mas vaccination of ch ld en and adults against poliomyel tis, the incidence of cutaneous eruption is ex tremely low George M Stroud, Harold L. Brodell, W ll m P Lascheid and Lew W Potts (Un Hospitals Cle e

3) Brit. J. Ven. Dis. 33 209 214, December 195
) J. M A 14 35 Jan 1958

land) report 12 cases Most dermatoses were fairly severe but none was serious and all subsided Seven of the 12 patients had received penicillin previously One was sensitive and another questionably allergic to it Nine had dermatoses considered to have important allergic components

Urticaria occurred in 4 cases. In Case 1 the patient had had mild urticaria before he received Salk vaccine, but a sharp attack occurred 6 days after the first injection. After a vaccine with a substantially lower penicillin content was used a month later no urticaria developed In Case 2 a girl 3 had fever malaise and urticaria after every Salk vaccine injection and also after an injection of diphtheria, pertussis and tetanus vaccine and toxoids which contained no penicillin. In Cases 3 and 4 the patients had a delayed type of allergic eruption with urticaria joint pains and a constitutional reaction

An eczematous eruption appeared to be precipitated, reproduced or exacerbated by inoculation against poliomyelitis in Cases 5 through 9 The incubation period in this group was shortest averaging 4 days Only 1 of the 5 patients was known to have received penicillin before and he had no history of previous sensitization This was the only patient in the group to be revaccinated and the eruption reappeared after the second injection of Salk vaccine

In Case 10 man 36 had a psoriasiform eruption after taking penicillin for a severe upper respiratory infection After an injection of Salk vaccine which contained the standard amount of penicillin he experienced a similar attack In Case 11 the patient a sister of the patient in Case 10 had an acute erupti [illegible] extrem ities a [illegible] Case [illegible] of her psoriasiform dermatitis soon after receiving an injection of Salk vaccine.

Contrasted with some cases reported in this study most penicillin reactors and persons with eczema and psoriasis were vaccinated against poliomyelitis without untoward reactions. Salk vaccine is suspect in the reported eruptions but if it is responsible, the causative ingredient or ingredients cannot be determined from the data submitted

► [Although the agent causing the reactions *following administration of*

the Salk vaccine is not known for all the patients presented, the fact that it was the penicillin in the vaccine which was responsible in some instances should alert physicians to be prepared for counteracting untoward reactions not only to the "active" ingredient but also to adjuvant materials or contaminants (silk!) contained in drug (see Brown, et al, J.A.M.A. 165 2178, 1957) —Eds]

Penicillin Combined with Gamma Globulin as Diagnostic Agent in Urticaria of Serum Sickness Type Due to Penicillin. George Rajka, Jr and Elizabeth Vincze[5] (Stockholm) found that 0.05 ml. of a mixture containing 10,000 I.U. of crystalline penicillin and 1 ml. of 10% gamma globulin was more effective than crystalline pen cillin alone for diagnosing urticaria of the serum sickness type due to penicillin. In 34 of 40 cases, intracutaneous reactions were obtained with the combined testing agent, compared with 16 with crystallin pen cilli alone. The combined agent did not produce pseudopositive reactions in doubtful or negative cases of pen cillin allergy or in controls

Reaction was mmediate in about 75% of patients who had reactions to the gamma globulin-penicillin combination. When a preparation that had been stored for more than 3 weeks and had become moderately opalescent was used rea tion was seldom immediate, but delayed or doubtful reactions ncreased. This confirms that the purer an allergen is the mo e lik ly eactions are to be immediate Frequently both immediate and delayed reactions occurred in the same per son The autho ha e no explanation for this.

In 9 of 18 passive transfer tests, the gamma globulin-peni cill n combination yielded a positi e eaction and in 4 a do btful reaction compared to only 2 positive reactions and 1 doubtful reaction obtained with penicillin alone. Of 6 patients who showed both immediate and delayed intracutaneous eactions, 5 showed passive transfer reactions the 6th had a doubtful reaction Of 5 patients who had only immediat ntracutaneo s reactions, 1 had passive transfer reaction and had doubtful reactions. Of 6 patients who showed only delayed ntracutaneous reactions, 2 had passive transfer reactions and 1 doubtful eaction One patient who had no intracutaneous reactio had a transfer eaction. Hence there was no correlation between Prausnitz Kustner eactions and immediate or delayed intracutaneous eactions.

► [The occurrence of positive passive transfer tests with the serums of

5) Ann Allergy 29 396, May June, 958.

subjects who had only delayed positive reactions and 1 subject who had neither an immediate nor a delayed intracutaneous reaction is most unusual.]—Eds.]

Visceral Lupus Erythematosus as Side Effect of Treatment with Hydantoin Derivates is discussed by H. Rupph and R. Vossen.* Hydantoin derivates have been used for years in treating epilepsy because of their reliable anticonvulsive effect. The most commonly used compounds are 5,5-diphenylhydantoin and 3-methyl 5 5 phenylethylhydantoin (Mesantoin) administered singly or combined with other antiepileptic drugs.

The following side effects to hydantoin therapy have been described previously: skin changes (exanthema), gum changes (hyperplasia), generalized swelling of the lymph nodes, gastrointestinal disturbances, central nervous system involvement (somnolence, dizziness, ataxia, tremor), vascular changes as periarteritis nodosa and liver damage (central lobular necrosis). Occasionally the blood of hydantoin treated epileptics has shown a positive L.E. phenomenon.

The authors describe 7 patients, 5 females and 2 males aged 11-63, in whom after varying periods of treatment with hydantoin derivates visceral lupus erythematosus developed with positive L.E. phenomenon in the blood. In the following 3 the disease was fully developed clinically, whereas the other patients had only subclinical manifestations.

CASE 1.—Woman epileptic 22, received 500 gm. Mesantoin in 3 years. During the last year her general condition deteriorated and she lost 10 kg. body weight. Joint pains and swelling of the foot joint developed. Finally septic temperatures set in, the finger joints swelled, and exanthema appeared on the head, neck, trunk, upper arm and hands. There was pleural effusion on the right, leukopenia advancing almost to agranulocytosis, a very high sedimentation rate, an increase in alpha and gamma globulin, and positive L.E. cells in the blood. After Mesantoin was discontinued and Ultracorten* administered for 1 month, there was striking improvement. After 3 months, recovery was complete. Only the L.E. phenomenon remained positive after 4 months.

CASE 2.—Woman epileptic, 63, received in 6 years about 240 Gm. Mesantoin and 500 Gm. diphenylhydantoin. Five months after resuming Mesantoin therapy she became ill with attacks of fever, exudative pleurisy, joint swelling and pain and skin changes. The sedimentation rate was high, the alpha and gamma globulins were increased and the blood showed positive L.E. phenomenon.

CASE 3.—Man, 55, with presenile depression, received, in preparation

(*) Schweiz med Wchnschr 87 1555-1558, Dec 21 1957

tion for electric shock therapy 4.4 Gm. Mesantoin in 9 days. On the last day he had high temperature, morbilliform exanthema, lymph node swelling and a greatly increased sedimentation rate. One week later bilateral pleural exudate pulmonary infiltration and transitory leukopenia developed. The alpha and gamma globulins were increased. The blood showed a positive L.E. phenomenon. After the discontinuance of Mesantoin and under penicillin and sulfonamide therapy all symptoms and signs subsided fast.

Most authors have assumed that pathogenically visceral lupus erythematosus consists of an antigen-antibody reaction with the formation of autoantibodies, which in vivo change the collagen connective tissue and, in vitro produce the L.E. phenomenon. In this reactive system drugs may act as haptens.

► [We do not believe it is desirable to label patients as having visceral lupus erythematosus in those cases in which certain medicaments (e.g. Mesantoin) produce the signs and symptoms of subacute and acute lupus erythematosus, including a positive L.E. cell phenomenon. It would be preferable to refer to such syndromes as lupus erythematosus-like drug reactions due to Mesantoin.—Eds.]

Eczematous Complications in Treatment of Tuberculosis Eruptions Resulting from Combined Aminosalicylic Acid, Dihydrostreptomycin and Isoniazid Therapy were observed in 37 patients by John T. Crissey, Earl D. Osborne and James W. Jordon (Buffalo). The lesions resembled nummular eczema, seborrheic dermatitis or a combination of both. The initial lesion in the form resembling nummular dermatitis (12 cases) were closely aggregated pruritic erythematous papules or papulovesicles, which coalesced rapidly to form coin-shaped eczematous plaques. The sites most commonly involved were the lower parts of the leg especially about the malleoli, the extensor aspects of the arms, the anterior axillary folds, the antecubital fossae, the dorsa of the hands and feet, the chest and the back. The lesions were often localized in areas previously occupied by other dermatoses such as stasis dermatitis, dyshidrosis, dermatophytosis or dermatitis venenata, though these conditions had been absent for many years. Lesions that had been present for some time gradually became thickened and assumed the form of lichen simplex chronicus.

The earliest change in the form resembling seborrheic dermatitis (6 cases) was the appearance of fine scaliness on the scalp, especially at the hairline. Later erythema appeared

(7) J.A.M.A. 143:1336-1338, Nov. 21, 1957

and the eruption spread to the external auditory meatus, retroauricular areas eyebrows nasolabial folds and occasionally the presternal area. The lesions then became moist, so that the picture closely resembled the exudative phase of seborrheic dermatitis except for response to treatment. Itching was often intense and complicating pyoderma was common The commonest eruption was mixed resembling both nummular and seborrheic dermatitis (19 cases) In 2 such cases the lesions progressed to a generalized exfoliative dermatitis

Since the eczematous eruptions in patients treated with chemotherapeutic agents resembled so closely the common skin diseases nummular dermatitis and seborrheic dermatitis, a definite relation to the antituberculous medications could be established only by prolonged observations. By observing the drugs being given when the eruptions began and the response of the eruptions to selective withdrawal of the drugs the authors concluded that aminosalicylic acid was the chief cause, that dihydrostreptomycin was an occasional cause and sometimes a prolonging factor and that isoniazid was not involved From the frequent finding of dihydrostreptomycin resistant micrococci in the skin lesions the authors postulated that a disturbance in the normal bacteriologic flora of the skin might underlie the eruptions

Management included an initial attempt at control by topical means without stopping administration of any of the tuberculosis drugs. If symptoms became unbearable or if alarming extension of the eruption occurred aminosalicylic acid was withdrawn On this regimen many reactions subsided. In severe cases, steroids were used combined with the chemotherapeutic agents

► [Without the detailed observations of Crissey Osborne and Jordon, implicating para-aminosalicylic acid as the principal cause of these eruptions, one would have thought that the dihydrostreptomycin was their cause. Topically applied neomycin frequently causes seborrheic dermatitis like or psoriasiform eruptions and, as was shown by Sidi et al there is an immunochemical relation between streptomycin and neomycin Previous reports of eruptions due to para-aminosalicylic acid dealt with scarlatiniform and urticarial eruptions —F J]

Cutaneous Reactions Due to Sulfamethoxypyridazine Donald G Lindsay (Ventura Calif) Isaac Firlina (Virginia Minn) Arthur J Bischoff and S William Becker Sr (Long

(8) A.M.A. Arch Dermat. 78 299-303, September 1 58

Beach, Calif.) report the occurrence of an erythematous maculopapular dermatitis in 13 of 85 patients (15.3%) taking sulfamethoxypyridazine. In 1 patient the dermatitis progressed to a severe, generalized, bullous and ecchymotic eruption. In the other patients the eruption cleared promptly when the drug was discontinued. Of the 13 patients with sulfonamide dermatitis, 5 had taken sulfonamides previously. Of the 72 who showed no reaction to sulfamethoxypyridazine, 29 had taken sulfonamides previously. Of the total 85 patients taking sulfamethoxypyridazine 2 (6.6%) of 30 taking 0.5 Gm. daily doses showed an untoward reaction, while 11 (20%) of 55 patients taking 1 Gm. or more daily had dermatitis. In general, dermatitis occurred within the first 5 days in patients who had taken sulfonamides previously and after about 2 weeks in patients with no previous experience with these drugs.

Daily serum sulfamethoxypyridazine determinations did not show a gradual increase with time at a constant dosage but averaged around 10 mg./100 ml. in patients taking 1 Gm. daily doses and 5 mg./100 ml. in those receiving 0.5 Gm. daily. No correlation between reactions and serum levels of the drug was possible, because too few determinations were made.

► [The principal advantage of this sulfonamide (Kynex®) is that adequate blood levels can be maintained with 1 or 2 doses daily. It appears doubtful that this convenience of administration is worth risking when the incidence of drug eruptions from its use is greater than 10%.—Eds.]

Melanosis Due to Camoquin was observed by E. Young[9] (Univ. of Utrecht) in 3 cases within a short period. Yellow scleras were also present, and 1 patient exhibited partial pigmentation of oral and vulvar mucosa. Skin biopsies showed an abnormally high melanin content, mainly in the epidermis but also in the cutis. The pigmentation may have been due partly to the Camoquin itself.

Man, 43, had taken 300-400 mg. Camoquin daily for almost 4 months for chronic lupus erythematosus. When examined, he exhibited brownish yellow color of the face, neck (Fig. 8) and dorsal surfaces of both hands and forearms. Covered portions of the body were less strongly pigmented. The scleras were yellow, the mucous membranes showed no pigmentation. The patient said that pigmentation had increased within a few weeks. There were no subjective symp-

(9) Nederl. tijdschr. geneesk. 102:1083, 1092, June ... 1958.



Fig 8 White plaque on right under j caused by lupus erythematosus, and pigmentation of face and neck (Courtesy of Young E Nederl. tijdschr geneesk. 102 1088-1093, June 7 1958)

toms. Camoquin® therapy wa topped immediately Further studies showed no evidence of icteru liver function tests and proteins were normal Serologic test were negative The scleral color was attributed to Camoquin® The skin color cleared after withdrawal of the drug

Hypervitaminosis A—Toxic Reaction. D W Creek, K. J McNiece and L. M Nelson[1] (Santa Barbara, Calif) report toxic manifestation resulting from prolonged and excessive ingestion of vitamin A in 3 patients

CASE 1 —Girl, 16 wa given 50 000 unit of vitan in A 3 times daily for acne vulgaris. On her own initiat e without medical upervision, she continued to take 150 000 unit of tamin A daily for over years. Because she began to lose her hair the ntak of vitamin A was stopped immediately Two month later her hair ha l topped fall ing out, but 1 year later although she wa much mpr ed it had not returned to its original thicknes The pat ent als experienced anorexia, loss of weight and epi tax which per i ted unt l the tamin A intake was liscontinued.

CASE 2.—Man 47 took 200 000 unit of v tam n A la ly for generalized dry scaly dermatitis. After 27 month on thi dosag several large ecchymotic area appeared on hi xtrem ties. Bleeding t me and clot retraction time were prolonged and the blood platelet count was 100 000. Three weeks after vitamin A wa l scont nued, the plate-

(1) Am. J Gastroenterol. 25 169-172 February 1958

let count was 147,000, the bleeding time was 1 minute and clot retraction time was normal. There was no further tendency toward hemorrhage

CASE 3 —Man, 67 had taken 200 000 units of vitamin A daily for 6 years. He stated that his gums had bled intermittently for 3-4 years, with profuse bleeding during dental extractions. Blood counts, bleeding and clotting time, prothrombin time, clot retraction and other laboratory tests were normal. Four months after vitamin A was discontinued, the remaining teeth were extracted without unusual bleeding He had no further hemorrhagic tendencies and remained asymptomatic

► [It is noteworthy that these 3 patients took much greater doses of vitamin A than those normally prescribed by responsible physicians. It is probably safe to surmise that in this era of indiscriminate intake of vitamins, many persons have undetected manifestations of hypervitaminosis A It should be remembered that the oil-soluble vitamins A and D can produce toxic manifestations if taken in large enough doses for sufficiently long periods When prescribing vitamin A it would be wise to limit the prescription and to advise the patient regarding the proper use of this vitamin —Eds]

Severe Acidoketosis in Two Cases of Psoriatic Erythroderma Treated by Cutaneous Application of Salicylic Acid in "Penetrating" Fat Base is reported by E. Sid A. Remberg M Hincky and J Bourgeois-Spinasse[2] (Paris)

CASE 1 —Young woman, 33 whose general condition was poor had resistant psoriasis. She was treated at home with salicylic acid in transesterified, hydrogenated triglycerides (TTH) the only treatment the skin would tolerate. This local treatment was continued after hospitalization besides oral medication with delta-cortisone and dihydrotachysterol. General treatment was interrupted on the 20th day because of asthenia, but local treatment with salicylated TTH was continued. Four days later acidosis and coma supervened suddenly accompanied by Kussmaul dyspnea, ketonemia and ketonuria, decrease in alkaline reserve, moderate elevation of urea and glucose and potassium in the blood. The patient died despite administration of glucose and bicarbonate solutions.

CASE 2—Man, 50, with generalized psoriasis, was treated on half the cutaneous lesions by salicylated lard and on the other half by salicylated TTH. Four days after beginning these applications, a precomatose ketosis developed, with ketonuria, decrease in alkaline reserve, moderate increase of blood sugar and urea and significant salicyluria. Improvement eventuating in cure of the intoxication began after cessation of local treatment. Salicylated petrolatum administered later caused no complications

The mixture of animal and vegetable triglycerides (TTH) is widely used by dermatologists because it is easy to use in preparation and application of ointments, it is penetrating and produces no irritation or sensitization. It was used by the

(2) Presse med 66 35 37 Apr 24, 1958

authors in over 160 patients and in several hundred cases by others with no ill effects until these 2 cases were observed.

Although the penetrating effect of TTH has distinct therapeutic advantages it also calls for caution when used to introduce substances that may be toxic in large doses. An experimental comparison on 3 subjects of a petrolatum and a TTH pomade containing 1 5 Gm salicylic acid, showed that blood salicylate 3 hours after application was 77.5 ± 5 mg/L. with TTH and 30 5 ± 5 mg with petrolatum a difference of 60% Risk of drug accumulation is increased in sensitive skins of children or in those with extensive skin lesions, as in psoriasis. When such skin treatments are contemplated with use of an active or potentially toxic ingredient it is necessary to consider the extent of the area to be treated concentration of the active substance in the ointment and the age general condition and individual reaction of the patient

► [The fact that the active ingredient incorporated in lotions, creams, ointment or other vehicles may be absorbed through the skin and then prove harmful systemically must always be kept in mind This pertains in particular to phenol and phenolic compounds such as resorcin and tars, ammoniated mercury chrysarobin, salicylic acid and even boric acid. Dermatologic therapy should take into consideration the skin site where the pharmacologic action of the topical medicament is desired Very often superficial action is preferable to deep penetration —Eds]

Parathion Residues as Cause of Poisoning in Crop Workers is discussed by Griffith E Quinby (Wenatchee Wash) and Allen B Lemmon[3] (Sacramento Calif) The residue left after application of parathion as a pesticidal spray in fields and orchards declines rapidly on most crops for the first few days and more gradually during ensuing weeks. Mild poisonings have been caused in workers thinning picking cultivating or irrigating crops of apples pears grapes oranges and hops treated with 1 lb/acre or more of parathion Several known instances of poisoning involved exposure to foliage or fruit sprayed not more than 2 days before However contact with trees and vines has caused poisoning as much as 12, 17 and 33 days after application of parathion In the episode occurring 33 days after spraying 16 workers in a vineyard were involved and the cause of illness was confirmed by low cholinesterase values and relief of symptoms by atropine The causal relation was further supported by the finding of a residue of 8 ppm parathion on the leave

(3) J A M A 166 740 44, Feb 15 1958

Although the vapor pressure of technical parathion doubles with a rise of temperature from 68 to 79 F the vapor pressure even at 103 F is only 1 μ Hg which is capable of producing at most a concentration of only 15 μg/L air It would seem most u likely that workmen would be subjected to such saturated air for prolonged periods, if at all However all thinners and harvesters have extensive contact between the fruit and their hands and less extensive contact between their arms and other parts of their body and the foliage Experiments have shown that the skin is the principal route of absorption e en duri g actual praying or aerosol operations. Therefore it seems almost certa n that dermal contact is more important than inhalation in the poisonings resulting from residues. No one has estimated the importance of oral exposure resulting from eati g drinking or smoking without washing the hand or from eating fruit while harvesting Dermal absorption is increased by removing shirts and other protecti e clothing and by wearing contam nated clothing for several days at a time.

All outbreaks so far recorded have occurred from residues deposited on f liage at least chest high. This may imply that workers are poisoned in this way only when dusted or bathed in the dilute residues practically from head to foot. After 7 years of parathion use, the lack of poison ngs from residues on lower row crops appears significant.

The chief symptoms of parathion poisoning re headache, nausea, om ting diarrhea, miosis weakness and mild shock. Poisoning due to residues on foliage has been relatively milder with more gradual onset than that produced by exposure during spraying or dusting The elati e m ldness of the illness due to residues has probably caused many physicians to attribute such llness to causes other than the insecticides to wh ch the crop workers were exposed. Because of the paucity of published reports of poisoning by residues physicians ha e heretofore tended to insist on a history of direct expos re to sprays, concentrates or dusts before considering a diagnosis of parathion poisoning Regulations n tended to minimize the hazards of using parathion need to be reviewed with respect to the poisonings that have occurred from the persistence of toxic residues.

* (Parathion is 0,0-diethyl-0-p-nitrophenyl thiophosphate This cholines-

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(3) J A M A 166 740 46, Feb 15 1958.

there is hyperkeratosis. This suggests that arsenic is bound in the keratin moiety.

On the basis of his findings, Scott proposes that, in a person with a history of arsenical therapy and a persistently high skin content of arsenic administration of BAL should be considered to aid elimination of residual arsenic and thereby reduce the chances of development of malignant skin changes.

[The high levels of arsenic in the skin and especially in the epitheliomas and keratoses of these patients seem to settle the old argument whether increased quantities of this element are present in arsenical keratoses and epitheliomas. Without examination of more patients who only recently have received arsenic it is not possible to decide whether there are significant personal variations in the ability to eliminate arsenic.—Eds.]

Arsenical Keratoses Associated with Carcinomas of Internal Organs. Cases of visceral cancer after ingestion of, or exposure to arsenic have been rare, and definite evidence of arsenic being the direct cause of carcinoma in internal organs has never been presented. M. Rosset[3] (St. Joseph's Hosp., Toronto) presents 2 cases of arsenical keratoses associated with visceral cancer. One man, 51, with cirrhosis and primary carcinoma of the liver had taken Fowler's solution for psoriasis, off and on for about 20 years. Another man, 38, with primary carcinoma of the head of the pancreas, denied ingestion of arsenic but stated that in adolescence he worked on a farm where he used lead arsenate to spray potatoes. The keratotic lesions on his palms appeared first while he was in his teens.

In both these, as in all cases reported previously, the possibility of coincidence of arsenical poisoning and internal carcinoma cannot be ruled out. However, the carcinogenic properties of arsenic have long been recognized, though experiments with it have produced only a few skin and other cancers in animals. In some cases reported in the literature minute doses of arsenic have produced evidence of intoxication; in others, signs of intoxication have not appeared until many years after the medication had been discontinued and the patients were probably out of sight of their attending physician.

Rosset feels that the benefits derived from arsenic in nonfatal diseases are not worth the risk of remote serious and

[3] Canad. M. A. J. 78: 416-419, Mar. 15, 1958.

terase inhibitor apparently does not cause any visible cutaneous damage, even though it exerts its poisoning effects via absorption through the skin —Eds.]

Retention of Arsenic in Late Cutaneous Complications of Its Administration. Until recently the smallness of pieces of skin available for analysis has limited the accuracy of methods for the chemical estimation of arsenic in that tissue. By inducing radioactivity of the arsenic by irradiation in an atomic pile for 24 hours this problem can be circumvented, provided standard weights of arsenic are irradiated at the same time. Since all the other elements found in skin have a comparatively low specific activity and long half life the skin radioactivity detected by this method is attributable solely to its arsenic content The applicability of this method is limited to tissue which do not contain elements closely resembling arsenic in their radioactive isotopes

Using this method of measuring arsenic content A Scott[4] (St. Bartholomew s Hosp London) found 0 4-1 μg arsenic/Gm wet weight tissue in samples of normal skin from patients with no history of arsenic intake In 7 of 9 epitheliomas removed from arsenic treated patients the arsenic content was over 1.8 μg /Gm The other 2 lesions gave values of 1 μg /Gm Two of 3 keratoses removed from arsenic treated patients had values over 2 μg /Gm Three of 4 biopsy specimens with the highest arsenic content were hyperkeratotic In 2 of 3 specimens of apparently normal skin of patients with a history of arsenic intake, the arsenic content was greater than normal—1.8 and 2 μg /Gm Epitheliomas removed from 2 patients who had been exposed to external contact with arsenic for at least 20 years showed a high arsenic content (5.7 and 7.2 μg /Gm) despite a lapse of 10 and 25 years respectively since last exposure A specimen of normal skin removed from 1 of these patients contained 1.9 μg arsenic/Gm

The quantity of arsenic retained in the skin apparently bears no precise relation to the duration of intake of the drug nor to the time lapse since cessation of therapy This suggests a personal variation in ability to eliminate arsenic In patients who have taken arsenic the content of this element is greater in sites in which epitheliomas have developed than in the rest of the skin Levels are particularly high where

(4) Brit. J Dermat 70 195-200 June, 1958.

the authors experience, blood boric acid levels in fatal poisonings are of the magnitude of 50-100 mg./100 ml. or more.

► [There is no particular merit in the topical use of boric acid solution and boric acid ointment as compared with saline solution and plain white petrolatum or white petrolatum medicated with agents which lack systemic toxicity (e.g. Sterosan® Vioform). Why then take chances on accidental or the undoubtedly very rare therapeutic poisoning from boric acid? —Eds.]

Nephelometric Studies in Drug Allergies were conducted by G. Ziegler[7] (Univ. of Basel). Various tests have been developed to demonstrate allergens in vivo or in vitro. In sensitized subjects the number of thrombocytes in the peripheral blood decreases more than 15% after exposure to relatively small amounts of allergens. This test has been found positive with inhalation, food and drug allergens. This method can be applied also in vitro by adding various allergen dilutions to the oxalated blood of sensitized subjects on a glass slide. In a positive test, agglutination of thrombocytes can be observed. This agglutination depends on two serum factors both thermolabile. The specific factor I is dialyzable through cellophane membrane, whereas the nonspecific factor II is nondialyzable and can be found in unsensitized persons. Since the origin of the thrombocytes did not matter it was felt that they acted only as passive indicators.

Because the above test is based on a discrete thrombo-agglutination which cannot always be recognized easily, it has been tried to measure a positive reaction photometrically with the aid of a sensitive nephelometer. With this method it became possible to visualize even slight turbidity in the plasma as well as in the serum of sensitized persons, after addition of the allergen in proper dilution. The previously mentioned factors I and II are responsible for this reaction. Serum factor III was found to be the cause for inactivation of factor I in about 6-8 hours after the blood was drawn. Factor III has two components, one blocks factor II specifically and the other neutralizes the respective allergen.

The author tried the nephelometric reaction on 22 patients with drug allergies. In 19 the responsible drug was determined with certainty. However, the nephelometric reaction with the corresponding substance was positive only in 1 patient who had severe Pyramidon® hypersensitivity. The

[7] Schweiz. med. Wchnschr. 84:525-527, Sept. 25, 1954.

even fatal complications from such treatment. Even when the dose of arsenic is carefully controlled, the physician cannot be sure how much exposure to it has occurred in a patient in the past.

It has been the routine practice of dermatologists to follow arsenical keratoses to detect signs of cutaneous malignancy. In view of the possibility of internal carcinoma or liver damage, internists also should follow such patients regularly with liver function tests, chest films and gastrointestinal series. Even if only an occasional case of cirrhosis or early carcinoma is detected, the trouble would be worth taking. It might also lead to discovery of more cases, unreported or never coming to autopsy, and bring forward more evidence of the carcinogenic action of arsenic.

► [The evidence that the internal carcinomas in these 2 cases were a consequence of the arsenic ingestion is not conclusive. Over the years literally hundreds and thousands of patients who have received arsenical therapy have been examined for various skin lesions resulting from such treatment. If internal carcinomas were definitely associated with the previous administration of arsenicals, one would expect that many more cases of carcinoma of internal organs would have reported in the past. Nonetheless, we agree that physicians should be highly suspicious of internal carcinoma when elderly patients, in particular, present dermatologic evidences of chronic arsenic damage.—*Ed.*]

Blood Boron Levels in Human Infants. In 34 infants and young children under treatment for various skin disorders and exposed only to dietary boron, Russell S. Fisher and Henry C. Freimuth[6] (Univ. of Maryland) found the average blood boron concentration to be 0.25 μg./ml. The highest level was 1.25 μg. In 37 patients exposed to boron-containing medications as well as dietary boron, the average blood boron concentration was 0.2 μg./ml. and the highest level was 1.25 μg. These levels are not significantly different from those of the first group. One patient in the latter group had been given baths in boric acid solution 3 times a day for a week.

Two children who accidentally received a boric acid solution orally showed blood boric acid levels of 7.89 and 7.44 mg./100 ml., respectively. The amount shared by the 2 children was 5 oz. containing 1½ teaspoonfuls of boric acid. Both children had gastric lavage at the hospital. Neither exhibited any signs of boric acid toxicity at any time, though these levels are above those previously reported as fatal. In

(6) J. Invest. Dermat. 30:85-86, February, 1958.

greater in men (14%) than in women (5%). Men with both basal and squamous cell carcinomas had a greater chance of having a second squamous cell lesion than either men or women with only a single squamous cell carcinoma. These differences were not statistically significant.

Of the total of 413 patients 70% were men. Among patients with lesions only on exposed body surfaces 73.2% were men whereas among patients with lesions only on unexposed surfaces, 53.3% were men. These observations are consistent with the concept that the frequency of skin cancer is higher in men than it is in women as a result of environmental factors.

[The incidence of approximately 3% for metastasis of squamous cell epitheliomas seems somewhat high to us. Roswell Park Memorial Institute is known as a "cancer hospital" and this may account for a high content of patients who have old, invasive and therefore metastatic lesions of this type.

According to the authors the chances of metastases occurring after the treatment of prickle cell epitheliomas are very small if they have not occurred within 3 years. This is highly important from the follow-up viewpoint. Follow-up is a must for 3 years and is desirable, but not likely to yield positive findings, thereafter.

The differences in the incidence of carcinoma of the exposed skin surfaces of men as compared with women are notable. The principal environmental factor producing the higher incidence in men is likely to be exposure to sunlight. This indicates once more how unjustified it is at present to attempt to induce people to increase their tanning via increased exposures to sunlight after taking 8-methoxypsoralen tablets.—Eds.]

Basal Cell Carcinoma in Children. Harold L. Stern and George V. Webster[9] (Univ. of California, Los Angeles) report 3 cases occurring before age 15. Case 1 is described here.

Girl, 11, had discoloration of the right ala since age 6 weeks. At age 5 the area enlarged and was treated with radium. At age 10, skin planing was attempted and finally biopsy was performed. Diagnosis was basal cell carcinoma. Under general anesthesia the lesion was widely excised and a full-thickness postauricular skin graft was applied to the defect. The pathologic specimen showed typical basal cell carcinoma excised with adequate margins. There was no recurrence during 8 months of follow-up.

Although basal cell carcinoma is uncommon in children, it is probably more prevalent than generally realized. It is estimated that 0.5-1% of basal cell carcinoma occurs before age 15. Prompt biopsy of all suspicious skin lesions in children, and appropriate excision and plastic repair are recommended before the lesion progresses to wide destruction. Surgery provides a specimen that the pathologist can exam-

(9) Am. J. Surg. 96:445-447, September, 1958.

others gave negative or occasional positive reactions, which on repetition were regularly negative and thus cannot be considered as true positive

The reactions with serums of patients who had eczema, inhalation allergies or sensitivity to Trichophytin were always negative

► [The difference between the positive findings of Hougné and Storck and the almost negative findings of Ziegler will have to be resolved through further studies with the nephelometric method.—Eds.]

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5 CANCERS PRECANCERS OTHER TUMORS AND NEVI

Frequency and Risk of Metastases in Squamous Cell Carcinoma of Skin. Alfred D Katz Frederick Urbach and Abraham M Lilienfeld[8] (Roswell Park Mem'l Inst. Buffalo) investigated 413 patients with 601 squamous cell carcinomas of the skin during 1946-50 Lesions of the vermilion border of the lip were not counted in the total Patients with metastatic disease at admission (20 patients with 24 lesions) were not included in the calculation of the risk of metastasis The other 393 patients had 577 lesions 15 (2 6%) of which metastasized during a follow up of 5 years or more

In determining the probability of development of metastases the life table technic was used With this method the varying periods during which the patients were followed could be taken into account The probability that men with primary squamous cell carcinoma of the skin would have metastases was found to be 3 6% at the end of the 3d year and did not increase thereafter with time In women the probability was 3% Men with both squamous and basal cell carcinomas had a probability that metastases would develop that was lower (2.6%) than that for men with squamous cell carcinoma only The degree of difference was not statistically significant. No essential differences based on the sites involved were noted in the proportions of lesions that metastasized.

The probability that a patient with a primary squamous cell carcinoma of the skin would acquire further lesions was

(8) Cancer 10 1162-1166, Nov Dec., 1957

All sebaceous cysts surgically removed for whatever reason should be microscopically analyzed. In all older patients who have long-standing cysts with recent change or a history of previous cancer the cyst should be promptly and widely excised.

► [The incidence of malignancy in sebaceous cysts as reported in the literature varies greatly. If it is correct that these lesions are malignant in 3-5% of the cases, then they should be treated with caution because of their potential to undergo malignant degeneration.—Eds.]

Investigation of Possible Apocrine Gland Component in Basal Cell Epithelioma is reported by Margaret Gray Wood, Kachorn Pranich and Herman Beerman[3] (Univ. of Pennsylvania). The pilary system, the pilosebaceous anlage or primary epithelial germ often have been described as the source of basal cell epithelioma. If basal cell epitheliomas may only develop from primary epithelial germ, rather than from pluripotential cells in the epithelial or follicular basal cell layer, the glandular tissue in the tumor, if any morphologic or functional differentiation occurs, should show characteristics common to the apocrine gland. Conversely, if pluripotential cells are the ancestors of basal cell epitheliomas, any functional or developmental characteristics of a glandlike nature might be either eccrine or apocrine.

Functional or morphologic evidence of an apocrine gland component was sought by examination of 210 basal cell epitheliomas. In only 2 tumors was a cystic structure suggestive of apocrine gland morphology demonstrable. In both instances the structure was located deep in the tumor. Morphologically the size was comparable to that of dilated apocrine glands. At least part of the wall was lined with a row of cuboid cells with an outer layer of flatter cells suggestive of myoepithelial cells. Small cytoplasmic buds could be seen protruding into the lumen, further mimicking the appearance of apocrine glands. McManus-positive material was present in the stroma and formed a membrane along the external surface of the cyst. No McManus-positive material was found in the lumen or along the luminal surface of the epithelial cells.

There is thus some morphologic evidence that these cystic structures may represent apocrine gland differentiation. However, examination of the cells of basal cell epitheliomas

(3) J. Invest. Dermat. 30:27, 281, June, 1958

ine to establish the morphology and clearance of the margins of the lesion Radiation in children is somewhat hazardous because of the danger of arrest in growth of underlying bone. The resultant scar from radiation therapy is sometimes unsightly and requires plastic revision later

► [Two cases of basal cell epitheliomas in patients under age 15 have been seen in the Oncology Section of the New York Skin and Cancer Unit during the past 4 years.

One should have no difficulty guessing that this paper was written by surgeons. While radiation may not be the treatment of choice for basal cell epitheliomas in children, there are other simple, satisfactory measures for handling such lesions e.g., desiccation and curettage.—Eds.]

Carcinoma Arising in Sebaceous Cysts. Jack W Welch[1] (Hertzler Clinic, Halstead Kans) reports that of 239 consecutive cutaneous cysts removed surgically and examined microscopically 128 were benign sebaceous cysts 6 were carcinomas with definite origin in sebaceous cysts and 106 were epidermoid cysts of which 3 were malignant The incidence of malignant degeneration of sebaceous cysts was 4.7% In distinguishing between sebaceous and epidermoid cysts histologically if the wall of the cyst showed keratinization and if a stratum granulosum could be demonstrated, the cyst was considered epidermoid. The sebaceous cyst is filled with sebaceous cells and debris and frequently contains large amounts of cholesterol and crystals The cyst wall is smooth and definite sebaceous cells are identifiable in it. The wall is usually only a few layers thick and there is little or no keratinization

The average age of patients in this series was 64 Males predominated 2 1 Though the usual site of malignant sebaceous cysts is above the shoulder in this group 4 of 6 such cysts occurred below the neck line—3 on the thigh and 1 on the chest wall One patient had 2 malignant sebaceous cysts simultaneously Such an occurrence has not been reported previously

The longest follow up of patients in this series is 3 years and the shortest 3 months During this period there has been no evidence of recurrence or metastasis in patients with malignant cysts. Since these were all cases of early carcinomatous degeneration Broders grade 1 or 2 and since all cysts were completely removed no recurrences metastases or deaths from the disease are anticipated

(1) A.M.A. Arch. Surg 76:338-352, January 1958

All sebaceous cysts surgically removed for whatever reason should be microscopically analyzed. In all older patients who have long-standing cysts with recent change or a history of previous cancer the cyst should be promptly and widely excised.

► [The incidence of malignancy in sebaceous cysts as reported in the literature varies greatly. If it is correct that these lesions are malignant in 3-5% of the cases, then they should be treated with caution because of their potential to undergo malignant degeneration.—Eds.]

Investigation of Possible Apocrine Gland Component in Basal Cell Epithelioma is reported by Margaret Gray Wood, Kachorn Pranich and Herman Beerman[2] (Univ. of Pennsylvania). The piliary system, the pilosebaceous anlage or primary epithelial germ often have been described as the source of basal cell epithelioma. If basal cell epitheliomas may only develop from primary epithelial germ rather than from pluripotential cells in the epithelial or follicular basal cell layer, the glandular tissue in the tumor, if any morphologic or functional differentiation occurs, should show characteristics common to the apocrine gland. Conversely, if pluripotential cells are the ancestors of basal cell epitheliomas, any functional or developmental characteristics of a glandlike nature might be either eccrine or apocrine.

Functional or morphologic evidence of an apocrine gland component was sought by examination of 210 basal cell epitheliomas. In only 2 tumors was a cystic structure suggestive of apocrine gland morphology demonstrable. In both instances the structure was located deep in the tumor. Morphologically the structure was comparable to that of dilated apocrine glands. At least part of the wall was lined with a row of cuboidal cells with an outer layer of flatter cells suggestive of myoepithelial cells. Small cytoplasmic buds could be seen protruding into the lumen, further mimicking the appearance of apocrine glands. McManus-positive material was present in the stroma and formed a membrane along the external surface of the cyst. No McManus-positive material was found in the lumen or along the luminal surface of the epithelial cells.

There is thus some morphologic evidence that these cystic structures may represent apocrine gland differentiation. However, examination of the cells of basal cell epitheliomas

(2) J. Invest. Dermat. 30: 273-281, June, 1958.

for alkaline and acid phosphatase activity and for deposits of glycogen lipid and iron revealed no positive evidence of functional activity which could be unequivocally (or even tentatively) described as characteristic of eccrine or apocrine glands.

Patients with Multiple Skin Malignancies I Some Remarks on Immunobiology *Observation of patients with multiple skin malignancies has offered nothing of practical value to increase their resistance to development of new tumors. Leon Goldman[3] (Univ of Cincinnati) describes research being carried out in immunology in relation to skin cancer*

TECHNIC.—Tissue is removed with sterile precautions from a cutaneous cancer One portion is used for microscopic confirmation of diagnosis the other portion is put into a sterile container and kept in a freezer until preparation. The frozen tissue is ground in a small, sterile, glass grinder Saline is added to the ground mass and then a modified Freund adjuvant (8 parts paraffin base, Bayol F to 1 part wetting agent, Arlacel) The creamy mixture is checked for sterility then used for injection. Most patients are given 0 1-0.2 cc. intradermally once a week for varying periods. Serologic controls are carried out on patients being treated.

The study has been in progress for 6 months. Small nodules persist for months at the site of injection but no large abscesses have developed. Two instances of focal reaction in previous injection sites have been observed Progressive histologic study in these patients has shown perivascular reaction and edema suggestive of a tuberculin response Tissue eosinophilia has been observed in some sections

Studies have been carried out on 12 patients with multiple basal malignancies and 1 with multiple squamous cell tumors So far of course, there has been no demonstrable effect on the active malignancies of any of these patients There is no clinical evidence that there has been any activation of any of the lesions.

► [The role of immunologic factor and of host tumor relationships in malignancies is receiving increasing attention (see for example the Symposium on Immunology and Cancer Ann New York Acad Sc 69 525, 1957) Cutaneous cancers would appear to be especially suited for investigations in this field —Eds.]

Distribution of Skin Tumors of Sole of Foot. M Levene[4] (Manchester England) studied the distribution of 511 lesions of the foot seen *during 24 years Of 42 melanomas 28* were on the sole. Almost all these lesions were on the arch

(3) J Michigan M. Soc. 57 531-534 April, 1958
(4) Brit. M. J. 1 1519-1520, June 28, 1958

region of the sole and were not at sites of pressure or irrita tion due to weight bearing This suggests that much more must be learned before accepting pressure or irritation as the mechanism of spread of melanoma, at least in the early stages.

Squamous cell carcinomas occurred primarily on the weight-bearing areas of the sole (ball of foot and heel) as did planta warts and hyperkeratotic lesions. No basal cell car cinomas were noted. The incidence of squamous cell carcinoma of the foot was 1 4% of all squamous-cell lesions seen at the author's hospital duri g the same period. This low incidence plus the fact that squamous cell carcinoma was much more common n men than in women suggests that constant trauma of weight bearing and walking may not by itself be a prime fact r n carcinogenesis.

Unlike other lesions, angiomas of the foot often extended wide surfaces, frequently involving both the dorsum and sole Tumors arising n areas of pre-existing disease were scattered indiscriminately

► [The sharp differences between the favored locations of melanoma and squamous cell epitheliomas are surprising In our own experience, squamous cell epithelioma on the soles is very rare indeed. Basal cell epitheliomas of the soles are also rare but they do occur Tw cases seen at the New York Skin and Cancer Unit were reported by Pascher and Sims (A.M.A. Arch Dermat 69 475, 1954) —Eds.]

Skin Cancer Some Ethnic Differences. Samuel D Allison d K. L. Wong[1] (Honolulu) report 293 cases of skin cancer seen in residents of Honolulu County by dermatologists dur g 1955-56. The rate was 138/100,000 population for Cau casian and fo non-Caucasians, 3 1 or a ratio of approxi mately 45 1 The difference is highly significant. Differences n bserved rates among various non-Caucasian groups were not tatistically significant

The whit population of Hawaii apparently has more ma lignant neoplasms of the k n than do white populations of selected mai la d areas. Whereas the rate of 138/100,000 population i based on reports by dermatologists only com pri ng less than 2% of physicians n the rea, reports in the U ted States from every hospital and clinic and from over 94 of physicians indicate the rates to be 109/100,000 in Dallas, 90 n San Francisco and 39 in Philadelphia.

I the 293 cases reported from Honolulu County both

(1) A.M.A. Arch Dermat 76 37 739 December 1957

squamous cell and basal cell carcinomas occurred often on all parts of the body. In Hawaii physicians cannot rely on the location of lesions as an aid in determining the type.

► [Interesting figures concerning a highly important subject. Among the sources of error in these statistics are the facts that the dermatologists of Hawaii, while comprising 2% of the physicians in that area, were examining the patients with the *specific purpose* of recognizing and tabulating the various cancers of the skin and furthermore that it is difficult to accept that every hospital and clinic and from over 94% of the physicians actually reported correctly and completely regarding cancers of the skin in the particular mainland populations under study.—Eds.]

Carcinoma in Situ of Vulva. J. Donald Woodruff and Eva E. Hildebrandt[6] report 14 cases gathered from the files of Johns Hopkins Hospital. Average age of the patients was 53. 7 were aged 50 or less and 3 were under age 40. Pruritus and/or irritation was the presenting symptom in about half the patients. A "growth" was noted by 4 patients, soreness or pain by 2. In 1 the disease was discovered on routine examination. In 6 patients ulceration was present. Two had multiple lesions. In 5 the lesions were white or leukoplakic and in 3 granular. The microscopic picture varied strikingly. Except for the hyperkeratosis in the lesions with grossly whitish appearance and parakeratosis in the granular reddened lesions, there was no definite correlation between the gross and microscopic pictures. In 3 patients vulvar disease developed after radiation therapy for cervical cancer.

Treatment in 8 patients was simple vulvectomy. One inguinal lymphadenectomy was performed due to erroneous diagnosis of invasive carcinoma. In 6 only local excision was carried out. X-ray therapy was not used. Several patients followed less than 5 years have had no recurrence. Three patients died, 2 of carcinoma of the cervix and 1 of unassociated disease.

It seems apparent from the pronounced variation in gross and microscopic appearance of carcinoma in situ of the vulva that only by careful investigation of even the smallest lesion can these early vulvar malignancies be discovered. Local excision would seem adequate in many patients. However, such intraepithelial lesions may be of multicentric origin. Consequently, simple vulvectomy with thorough study of the tissue for evidences of invasive disease would be safer.

► [Surgery of vulvar lesions should not be undertaken without benefit of

(6) Obst. & Gynec. 12:414-424, October, 1958.

careful histologic diagnosis The decision as to what therapy should be initiated apparently presents difficulties for some physicians when vulvar changes other than malignancy are present. The article by Hyman and Falk (see chapter on Miscellaneous Dermatoses) sets forth some of the errors in management which are likely to take place unless the physician can differentiate the various eruptions which may occur on the vulva and is fully acquainted with the methods used in their care.—Eds]

Xeroderma Pigmentosum Report of Eight Cases of Mild to Moderate Type and Course Study of Response to Various Irradiations. Of the 8 patients seen by Chaim Berlin and A. Tager[7] (Tel Aviv Israel) 7 were Jews and 1 was an Arab All were dark complexioned with brown eyes and hair The face was most severely involved, though other uncovered parts were not free from lesions All patients presented various-sized freckles. They appeared early in life often in unusually large numbers. Their color was not uniform and varied from dark brown to coal black. Dirty brown to gray brown hyperkeratotic papules, 1-4 mm. in size sometimes of warty or tumor-like appearance, covered the face from time to time Several patients presented telangiectasia and small angiomas others had leukodermic spots which had resulted from removal of tumors.

One to many tumors were observed in 4 patients while they were under treatment. The tumors were located on the temple, eyelids, nose and cheeks and grew fairly rapidly Bleeding and ulceration were often present. In no instance was there evidence of involvement of regional lymph nodes.

Routine laboratory examinations were normal. Urinary porphyrin determinations were also normal. Two *patients* showed moderate and 4 extreme sensitivity to ultraviolet light. In 2 patients pigmentation persisted 9 months. Long lasting pigmentation was also produced by 100 r filtered and unfiltered x ray and by 100 r grenz rays. Therapeutic tests with corticotropin, chloroquine and vitamin A showed these agents were not beneficial.

► [The fact that apparently noninvolved skin of patients with xeroderma pigmentosum responds with more intense erythema and/or pigmentation following exposure to ultraviolet light, x-ray and grenz rays than does the skin of normal subjects leads one to speculate concerning the mechanism of these reactions Does this mean that the skin changes associated with xeroderma pigmentosum (which are considered to be precancerous) are not unlike those that might be produced by prolonged exposure to sunlight or threshold carcinogenic doses of ionizing radiation and that exposures to only small amounts of ultraviolet light or ionizing radiation have an addi-

(7) Dermatologica 117: 33, January 1958

tive effect, thus resulting in a more intense biologic reaction clinically? —Eds.]

Pre-existing Roentgen Ray Dermatitis in Patients with Skin Cancer Of 105 patients with skin cancer treated by Robert S Totten Philip G Antypas S Milton Dupertuis, John C Gaisford and William L White[8] (Univ of Pittsburgh) 20 gave a history of previous roentgen ray exposure All but 1 had definite clinical evidence of chronic radiodermatitis. In the patient with no such evidence there were histologic radiation changes in the skin surrounding the tumor Ten patients had received radiotherapy for acne and all had basal cell carcinoma on the face neck or shoulders Three patients were physicians whose hands were exposed during repeated fluoroscopic examinations Each had squamous cell carcinoma The other 7 patients had received radiotherapy for various benign conditions (eczema psoriasis fungous and toxic goiter) Three had squamous cell tumors and 4 had basal cell carcinomas on the face, neck trunk or extremities. Multiple and/or recurrent tumors occurred in 9 of the 20 patients. Two basal cell carcinomas were unusual widely infiltrating nonulcerating growths involving the upper lip and nose

The shortest interval between roentgen therapy and occurrence of tumor was 14 years and the mean was 25.2 years. Longer follow up of patients who have had 1 000 r or less and who have been said to be without complications might reveal the occurrence of tumors even in this group

The ultimate prognosis for patients with skin cancer in pre-existing roentgen ray dermatitis is probably worse than that for nonirradiated patients with similar tumors because of the high recurrence rate and the tendency for multiple tumors to develop The development of extensive tumors possibly can be reduced by careful periodic examinations early treatment of suspicious lesions and prophylactic removal of areas of radiodermatitis

► [In this study 85 of the patients with skin cancer had *not previously* received x radiation The information regarding previous exposure to x-ray was obtained on history alone and *nothing* is known about the *dose* received Furthermore it is of importance to know that all but 1 of the patients with a history of roentgen radiation showed definite clinical evidence of chronic radiodermatitis

It is noteworthy that 14 of 20 patients had basal cell epithelioma For

(8) Cancer 10 1024-1030 Sept-Oct 1957

merly the teaching was that roentgen-ray epitheliomas usually ar of the prickle cell variety, but several recent publications reported that this is incorrect and that basal cell epitheliomas not uncommonly arise in areas of radiodermatitis

W do not share the authors pessimistic anticipation that epitheliomas due to fractionated roentgen-ray doses totaling less than 1,000 r may also be found All evidence to date suggests strongly that if one stays below that dosage and if the treatments are given by the accepted technics, no radiodermatitis and therefore no epitheliomas will be produced However, are afraid that those who persist in giving much larger total doses of fractionated therapy for benign dermatoses take chance on producing sequelae Actually in the long run they may giv support to those who object even to any use of superficial -rays in the treatment of benign dermatoses —Eds]

Adenocarcinoma of Ovary Presenting as Acanthosis Nigricans. Though many cases of acanthosis nigricans and carcinoma have been reported, the association of this cutaneous



Fig 9 ages of left hand showing hyperkeratosis (Courtesy of Dingley E R, an Marten, R H J Obst & Gynaec Brit Emp 64 898-900 December 1957)

d sease with primary ovarian neoplasm ppears e tremely a e E. R. Dingl y and R. H Marten (King s College H sp London) report case.

Woman, 50, had had no ymptoms of ovarian disease t the time she examined because of cutaneous changes A typical lesion of acanthosis nigricans as present in the perianal region, with thick ening and brownish black discoloration of the skin in this area. The palms and the palmar surfaces of the fingers were dry coarsely hyperkeratotic (Fig 9) and yellow Similar but less marked changes

( ) J Obst & Gynaec Brit Emp 64 898-900, December 1957

were present on the soles. The finger nails were brittle and showed definite koilonychia. The dorsal surface of the tongue was rough and granular and showed deep transverse fissuring. Raised, rough, granular plaques were present on the inner surface of both cheeks. Biopsy of the perianal lesion showed a histologic picture compatible with a diagnosis of acanthosis nigricans.

No masses could be felt on abdominal palpation, but some free fluid was thought to be present in the peritoneal cavity. Pelvic examination revealed nodules in the pouch of Douglas. At laparotomy a papilliferous cyst was found in the right ovary with metastases in the pelvis and in the para-aortic and omental lymph nodes.

This patient had excessive lanugo hair over the face and neck. The abnormal hair growth appeared at the same time that other skin changes were first observed. The authors suggest that both the acanthosis nigricans and the hair growth may represent a response to some abnormal substance produced by the ovarian carcinoma.

► [Another instance in which cutaneous manifestation led to the diagnosis of internal disease. Findings such as these should alert the physician to be ever mindful of the hitherto inexplicable relationship of internal carcinoma and various changes in the skin.—Eds.]

Malignant Melanoma of Feet and Hands. According to Robert J. Booher and George T. Pack,[1] 16.5% of all malignant melanomas noted at the Memorial Cancer Center, New York, from 1935 to 1950 were on the hands and feet, though these surfaces constitute only 10.5% of the total body skin surface. There were 29 patients with melanomas of the hands and 122 with melanomas on the feet. About 60% of the lesions occurred in women. All but 2.5% of the patients were white.

Of the lesions on the feet, 68 occurred on the dorsum and 54 on the plantar surface. Only 30 lesions were apparently preceded by a mole of long standing or a birthmark. Of the 122 melanomas on the feet, 32 (26.2%) were treated by local excision alone, with a 5-year definitive cure rate of 34.4% (11 patients). The 5-year survival rate without recurrence for all malignant melanomas of the feet was 25.3%. In patients in whom groin metastases became evident during observation, an average of 20.7 months elapsed before metastatic lesions were detected.

In treatment of the primary lesion, subungual melanomas or those on digits were removed by disarticulation at the metatarsophalangeal joint or amputation through a metatarsal bone. Most of the other primary lesions were treated by

(1) Surgery 42:1084-1121, December, 1957.

wide excision and immediate application of a skin graft of intermediate thickness.

In radical groin dissections for proved metastases, the 10-year definitive cure rate was 10.9% (5 of 46 patients). The group of elective groin dissections without clinical evidence of metastases, but in which microscopic study revealed metastases yielded a 5-year definitive cure rate of 20% (1 of 5 patients). In electi e groin dissections without clinical evidence of metastases and in wh ch nodes were negative microscopically the 5-year cure rate was 40% (4 of 10 patients).

Of all who had surgery of the feet, 16.5% (20 patients) subsequently had local recurrence on the feet or widespread dissemination throughout the leg. Of all who had groin dissection, 25% (14 of 56 patients) had diffuse recurrence in the extrem ty or in the scar of the groin dissection.

The 5-year definitive cure rate as compared with the diameter of th primary melanomas were 1 cm., 29.4% (5 of 17 pat ents) 1-2 cm. 07% (6 of 29) 2-3 cm., 22.2% (2 of 9) 3-4 cm. 18.1% (2 of 11) and 4-5 cm., 10% (1 of 10). In 4 pa tient the pathologist noted vein invasion, 3 of whom died of melanoma, but 1 surv ed over 5 years without evidence of dissemination. Ulceration of the primary lesion or its absence was not specifically noted often enough to consider its influence on prognosis.

During 1935-47 melanomas of the feet with known metastases to the groin w re usually treated by excision and skin grafting or digital amputation for the primary lesion, and radi al groin dissection with preservation of the leg. The 5-year cure rate for melanomas so treated was never better than 14% An adequate conjo ned superficial and deep groin d ssection ine itably produced some blockage and lymph ta is which s the worst possible setting for residual mela noma in the leg resulting in diffuse melanomatosis by lymphatic tumo permeation. Amputation after this accident has pro ed futile. Recently melanoma of the foot has been treated b wide excision, w th mmediate superficial groin dissection. If metastases are found on frozen section analysis rad cal groi dissection is completed, but if not, the superficial groin dissection i deemed adequate.

In an experimental series of 13 patients with proved groin metastases 1 patient died of melanoma over 5 years after

amputation by hip-joint disarticulation combined with retroperitoneal lymph node dissection. Eleven patients died in less than 5 years and 1 is living and well over 5 years after surgery. The efficacy of this therapeutic approach in advanced cases remains to be proved, but if the end results are to be accepted as an improvement, such surgery must be done in an earlier phase of the disease than in the past.

Of the 29 patients with melanoma on the hands, 79.3% had lesions on the dorsal surface. In 10 treatment was confined to the hand; 4 (40%) of these survived 5 years. The 5-year definitive cure rate for malignant melanoma metastatic to the axilla was 16.6% (1 of 6 patients).

There were 29 subungual melanomas among the total of 151 patients. Two (15.4%) of 13 patients with subungual lesions on the fingers and 4 (25%) of 16 with subungual lesions on the toes had 5-year cures or more. It is surprising that although melanoma of the hand carries much better prognosis in general, this apparently does not hold true for subungual melanoma.

► [If only the knowledge derived from the numerous statistics given in this and other papers was of sufficient help to make possible an accurate clinical diagnosis of malignant melanoma!—Eds.]

Early Recognition of Melanoblastomas. N. Melczer and J. Kiss[2] (Univ. of Pecs) found that polarization resistance of the tissues, the so-called pseudoresistance, decreases measurably at onset of malignant transformations. According to the authors' method, with the aid of a direct-current tube amplifier and microvoltmeter, it is possible to determine within a few seconds and without biopsy whether a melanoma is benign or malignant. This electrometric method was used in over 400 patients with epithelial skin tumors and in

malignant melanomas, some of which were early lesion and some were fully developed, 21 juvenile melanoma, and 4 cases of Hutchinson's melanotic freckle.

Of 465 patients with pigmented nevi (junction and compound) none showed electrometric indication of malignancy, and readings were never over 4 mv. Patients with juvenile melanomas also had normal readings. All 14 patient with

(2) Dermatologica 117:243-252, October, 1958.

early or late malignant melanomas 2 of whom had the achromic form had greatly reduced polarization resistance. In early tumors, the read ng was 15-25 mv whereas in fully developed tumors, the read ng ranged from 20 to 40 m Of 4 patient with melanosis circumscripta praeblastomatosa in 1 partial malignant transf rmation was found. Biopsy after x ray treatment showed a malignant melanoma that had broken through the epidermal border

► [Methods suggested in the past for the diagnosis of malignant melanoma have failed to fulfil all of the claims made for them.—Eds]

Malignant Melanoma in Albino Report of Case is presented by T Elliott Young[3] (New England Deaconess Hosp Boston) Maligna t melanoma s far more frequent in light kinned races than in those with dark skin and has its h ghest incidence in blond persons w th pale skin. Despite this predilection for the light-skinned person, there has been no previous report of malignant melanoma in an albino

Mal gnant m lanoma is thought to arise from the melanin producing cells of the body In the epidermis these cells have been named melanodendrocytes (Becker) In completely nonpigmented skin, t might be thought that there are no m lanodendrocytes and theref re that albinos do not develop malignant melanoma because of the absence of these cells. Howev r studies of no pigmented skin by gold-impregna tio technics have revealed that n cases of vitiligo and al bin sm melanodendrocytes are present in normal numbers. Do pa and tyrosinase tests are negative. This suggests the nonpigmentation is due to a pathophysiologic defect in pig ment production

Most pathologists make the diagnosis of malignant mela noma without recourse to special staining technics. Only in am lanotic lesions without characteristic architecture, such m metastasis re special stains required for identifica tion f the tumor

If in an albino tumor were to arise from these c lls which ar phy siologically unabl to produce pigment, it would be natomicall identical with m lanoma Because of th defect in pigment production the u ual dopa and tyrosinase tests w uld not, h wever be pos ti e and the diagnosis would rest on the characteristic growth pattern.

Albino Caucasian woman, 40, had the primary lesion mole on

[3] A.M.A. Arch. Path. 64 54-191, August 57

amputation by hip-joint disarticulation combined with retroperitoneal lymph node dissection Eleven patients died in less than 5 years and 1 is living and well over 5 years after surgery The efficacy of this therapeutic approach in advanced cases remains to be proved but if the end results are to be accepted as an improvement such surgery must be done in an earlier phase of the disease than in the past.

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(2) Dermatologica 117:24 252, October 1958

Reticulosarcomatoses of Skin, according to Gerd Klaus Steigleder and Hans-Georg Hunscha (Univ of Frankfort) embrace diseases characteri ed by an increase in the connec ti e tissue cells that are not discernibly differentiated (therefore often called juvenile) These diseases are always lethal. There is no primary metabolic disturbance. Transitory re gression of some or all skin eruptions may occur The clinical picture is variable extending from flat scaling foci to eryth roderma and poikiloderma, from many papules to multiple tumors The same clinical appearanc does not mean the same histologic structure nor the same clinical course. In the recent literature these diseases have been called reticulosis ret culoendotheliosis, reticulosarcomatosis, etc.

Classification of the reticulosarcomatoses accord ng to his tologic struct re is not feasible for a number of reasons The cells of the infiltrates have been given names on the definition f which no consensus has been reached. The cells have been described according to subjective impressions. This becomes especially apparent in characterization of the chromatin tructure and nucleoli Unproved functional properties have been claimed for the cells. Reports rarely mention the meth od f pretreatment of the histologi sections. Staining of the n cleu and cell plasma, and also the nuclear structure great ly depends on the preceding type of fixation.

Mono- or polymorphism of an nfiltrate are not defined uniformly It has not been clearly expressed whether poly morphism in an infiltrate means a mixture of various cell types (filtrate polymorphism) o whether it denotes the great variability of a single cell type within an infiltrate (c llular polymorphism) Infiltrations should be called monomorphi only f the variations are n on single cell type, ffecting si nd shape. It is important to remember that mutual ex stence of cellular elements n the same infiltrate does not mean that these elements originate from each other Recently p esence of argentophil fibers has been stressed. It tremely difficult to decide whether these fibers are newly formed by the cell or whether the cells are only incidentally ttached t them.

It may become difficult to decide whethe an infiltrate con si t f one and the same cell type or of various cell types

) Arch. klin. u. exper. Dermat. 201: 11-444, 1955

her calf which began to increase in size and commenced to bleed. Metastases occurred to the cerebral cortex, hilar and axillary lymph nodes kidney and skin of the abdomen. Dopa tests on the metastatic lesions were negative. The primary lesion revealed the characteristic junctional activity and malignant nevus cells of a melanoma.

► [Unfortunately the author does not describe the clinical appearance of the mole from which the melanoma is said to have originated.—Eds]

Paget s Disease of Nipple Occurring in Young Woman Review of Literature. Reports of Paget s disease of the nipple before age 30 are rare. P R Joyce and J S. Lekias[4] (Perth) report a case in a woman which was clinically evident at age 28, but not diagnosed until 2 years later

Woman 30, noted cracking of the nipple during the 6th month of her 4th pregnancy Treatment resulted in temporary improvement, but 2 weeks after weaning of the infant, at age 4 months, cracking recurred. During the next 18 months a rash appeared around the nipple, and the nipple became eroded. Treatment was not beneficial. *Examination revealed a scaly crusted eruption involving the right* nipple and areola. The nipple was partially destroyed. There was a suggestion of a small tumor under the nipple but no deep masses or glands could be palpated Biopsy of the nipple revealed the classic changes of Paget's disease Radical mastectomy was performed. Sections from several different areas of the breast parenchyma, including a well-defined nodule close to the axillary tail, showed intraductal and early lobular carcinoma. One small deposit of intraductal carcinoma was found attached to the capsule of one of the axillary nodes. Paget s disease was extensive in the ep dermis of the nipple and areola and at the duct orifices. There was a discontinu ty between the intraductal carcinoma of the breast and that present in the nipple.

The histogenesis of Paget s disease of the nipple is controversial It is generally agreed that the epidermal changes in the nipple con titute intraepithelial carcinoma However some regard the malignant change as being of epidermal origin whereas others maintain that the carcinomatous cell are of duct origin The authors feel that Paget s di ea e is a manifestation of mammary carcinoma which is of a diffuse type and in cases seen at an early stage is intraductal and intradermal later to become inva ive

► [Although the histogenesi of Paget disease of the nipple remains controversial, the physician must consider any eczematous lesion of the nipple and areola as being Paget s disease unt l proved otherwise This does not mean that biopsy must be done in all such instances, as many of these eczematous lesions will respond promptly to appropriate topical mea ures If, however there is unsatisfactory response to treatment, a proper biopsy should be performed.—Eds]

(4) Australian & New Zealand J. Surg 28 45 4 August, 1958

Result of this study confirm the authors hypothesis that can ers may develop n fibromas. This causal relation was upported m some cases by macroscopic and histologic find ing cancer develop ng near fibroma, pendulous basaloma, epithelial d sorga zation on the surface of the fibroma and atyp cal epidermis In the Pinkus tumor there were premalignant lesions along ide the fibromatous structure. A definit relation between fibroma and cancer also was ug gested by the reported case of a planocellular epithelioma which progressed to a fibroepithelioma. Premicroscopic ulcers demon trate the existence of a premalignant or even malignant transf rmation. The authors p esent e perience however does not permit defin te conclusi ns as to the value of the colposcopic m thod in early diagnos s of precancerous lesions of keratotic cutaneous surfaces.

One important esult f this study was the discovery among the 91 cases of ? precancerous and 6 cancerous le ions. These find ngs demon trate that fibromas which appear clinically benign especially n regions exposed to prolonged irritation, can, at an ad anced age, be regarded as precancerous, and they often reveal true malignant degeneration

Keratosis Senilis Biologic Concept of Its Pathogenesis and Diagnosis Based on Study of Normal Epidermis and 1 730 Seborrheic and Senile Keratoses is presented by Herman Pi kus (W yne State Un v) Keratosis senilis is a disturbance n the normal symbiosis of malp ghian cell and d esal epith l um n the epidermis. The distu bed balance bel eved to be due to ngle epidermal cell undergoing heritable hanges that make them functionally inadequate increase their p l ferative tendencies nd, through progression lead t the d elopment of carcinoma in situ and freq ently t m as carcinoma

Exam nation f serial sectio of typical sen le keratoses and f senile km n the vicinity of senile keratoses reveal that the epiderm has lost its granular layer and para keratotic Th et Malpigh i consists of light-stai ing edem t m prickle ell that v ry somewhat in size and hape a d ha lost their orderly strat fied arrangement. The basal l yer does not u ually consist of small dark-staining pal sade

(mono- or polymorphic infiltrates) It is especially informative to compare the nucleoli found in the same infiltrates but which are subjected to various fixing fluids, such as Carnoy's Maximow's or 5% formaldehyde Fixation according to Maximow and staining by Giemsa are especially useful for assessing plasma staining Poorly differentiated connective tissue cells may appear in the same or similar form in various diseases. They have like the mycosis cells, little differential diagnostic value

Lidner and Meyer conclude from histochemical studies that destruction alone does not prove the malignant character of reticular new formations because the same changes may also be found in inflammatory diseases Steigleder and Schultis have searched for nonspecific esterases in reticulosarcomatoses and mycosis fungoides Neither the usual reactions nor by addition of or pretreatment with substances that stimulate or inhibit esterases was it possible to differentiate between reticulosarcomatoses mycosis fungoides and other specific or nonspecific infiltrations

Premicroscopic and Histologic Examination of Fibromas of Skin with Particular Reference to Their Precancerous Character T Venkei and J Sugar[6] (Budapest) report a study of 91 chronically irritated fibromatous lesion removed at the patients request for cosmetic reasons or because of susceptibility to trauma The surfaces of the lesions were stained and studied by means of Hinselmann's colposcope to discover signs indicating a precancerous or cancerous state.

The lesions could be classed in three groups fibromas confirmed by histologic examination (46) histologically verified cancers (16) and lesions with histologic diagnosis of nevus benign tumor etc (29) The reason for the relatively large discrepancy between clinical and histologic diagnoses (about 50%) was partly the lack or paucity of pigmentation of the nevi which therefore resembled certain semiglobular fibromas and solitary lesions observed often in benign tumors Macroscopic diagnosis of cancers resembling fibroma or developing in fibromatous terrain is not possible since the malignant portion is either a cancer at its onset or a microcancer

(6) Ann. dermat. 84:647 66, Nov Dec 195

encies for lateral spread normal symbiosis is replaced by a labile balance between contending epithelial groups. The outer surface becomes covered with keratinized, adnexal squamous epithelium whereas the diseased epidermis tends to undermine and creep along the dermoepidermal junction The normal vertical succession of cells is replaced in keratosis senilis by a lateral sliding of cells over and under each other

The characteristic changes are best recognized in well de eloped, flat, scaly lesions. Early changes consist of small groups of light-sta ning irregular cells, usually filling the space between two follicular ostia, or bordering with sharp delineation on normal skin. Advanced stages manifest a more pronounced atypical budding of anaplastic epidermis and its downward creeping around th adnexal cones, which t surrounds n a cuffl ke pattern. In some lesions the anaplastic epidermis is almost completely epressed from the open sur face In these in tances atypically keratini ed cells may be observed in the interepithelial cleft. Such lesions may re semble k ratosis f llicularis. In some examples of keratosis senilis the epiderm s becomes hyperplastic and almost ver rucous, nd the parakeratotic layer in many p les up and may form cutaneous horns.

Signs of beginning in asion, which eventually lead to full blown squamous cell carcinoma, are observed in three differ ent ma festations. Atypical budding of epidermis between ad exa may e tend deeper and deeper and eventually involve the pars eticularis of the corium. The cuffs around the ad nexa may l de down farther and become m as e, or the epidermis may encroach on the adnexal epithelium at the ostia, thereby cutting t off from the surface.

Attention di ected to the pathognomon c features described and to their p per nterpretation in biologic terms will esult in greater accuracy in histologic diagnos s of keratos sen lis In ma y instances diagnosis may be made from elatıv ly small amount of tissue emo ed for biopsy if the sharpl different types of ep thelium n their typical elation ar present Impend ng o accomplished progression to in asi ca cinoma can also be judged with increased as surance Differentiation from other keratoses, from basal cell

cells but of elements that resemble prickle cells. The dermoepidermal junction may be straight and the entire epidermis relatively thin or there may be irregular buds that extend downward In other instances the epidermis may be hyperplastic and acanthotic The regular pattern of rete ridges and papillae is lost. This altered "anaplastic" epithelium forms sharp borders against darker staining well-stratified and usually somewhat hyperplastic epithelium that manifests a hypertrophic multiple granular layer and hyperkeratosis. Study of serial sections reveals that the latter type of epi-

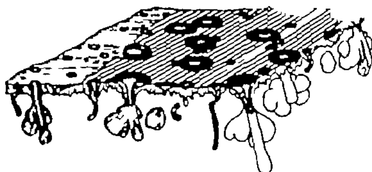


Fig 10 —Changes in keratosis senilis (Courtesy of Pinkus, H Am J Clin Path. 29 193-207 March, 1958)

thelium always lines pilosebaceous and eccrine ostia. A similarly sharp border is present at the periphery of the keratosis against the epidermis of the normal skin The dividing line is practically never vertical but is slanted, with the abnormal "native" epidermis extending farther at the dermal junction and the normal "adnexal" epidermis farther at the keratinized surface

The biologic significance of these features is demonstrated in Figure 10 The left side represents normal epidermis. Follicular and eccrine ostia are surrounded by thin tubes of adnexal epithelium The right part illustrates the concept that the epidermis in keratosis senilis has become anaplastic and biologically inadequate It is not recognized by the adnexal epithelium that begins to form epidermis as it would in the healing of wounds The adnexa build up hypertrophic inverted cones that tend to spread in an umbrella like pattern on the surface. Inasmuch as the surface is not actually denuded and the anaplastic epidermis also has increased tend

nevus cell pparently came from the periphery of the origi nal lesion.

It is deduced that the riginal lesion appeared cl nically as a complet ly benign common mol without a halo of pig mentation evident on examination This mole wa remo ed by ne f the common methods for cosmetic reasons. Pig ment recurred, causing anxiety to both patient and physician. Apparently when the pid rm s grew over the defect it car ried with it junction nevus cell wh ch prol ferated and pro d ced the recurrent lesion and repigmentation of the area.

The question of the prognost c ignificance of this process arises—whether this means activation of a quiescent nevus



Fig Recurrence of junction nevus (A) over incompletely removed pigmented intradermal nevus (B) Hematoxylin-eosin reduced from 0 (Courtesy of Schoenfeld J and Pinkus, H A M rch Dermat 78 30 35, July 1958)

implyi g pos bl 1 ogre n t a mal gnant state There no evidence of s ch impl catio in th s material o that todied by Walton He found that no junctional activ ty oc curred n ne u which did not how t n the original les on In none f th present cases were there any of the criteri m wh ch the diagnosi f mal gnancy in a cellula evu est There were no m toses n cells of unusual size d no rea t nflammatory infiltrat It seems, instead, that the evu el es earl part of ts natural history As ch ldren the finding f a ju ctio n ne us is the common pected occurrence a d does not mply malignant dev lop ment so here in you g epiderm nevu cells form junc t onal nests

It preferabl to exam ne microscopically at least th uperficial portion of nevi removed for cosmetic p rposes

epithelioma and from dermatoses such as lupus erythematosus is made more easily

The principal lesion from which keratosis senilis must be distinguished is seborrheic keratosis The latter is always a cutaneous papilloma that (1) consists of well-ordered epidermal cells without evidence of anaplasia and (2) manifests hyper rather than parakeratosis usually with the formation of deep keratin filled recesses or horny cysts in the substance of the hyperplastic epithelium. Hair follicles and sweat ducts if they pass through the seborrheic keratosis are usually difficult to recognize because their epithelial lining is similar to the surrounding mass of cells The basal layer is well preserved and no atypical budding occurs Inflammatory reaction is often completely lacking and senile elastosis is observed only beneath lesions that occur on the exposed surfaces

► [An excellent discussion of the histologic features of senile keratoses which should prove helpful, especially in cases in which it is impossible clinically to differentiate between senile and seborrheic keratoses. The fact that probably 15-20% of senile keratoses undergo malignant changes makes it necessary that these lesions be evaluated carefully on the basis of clinical appearance and that all those which no longer appear quiescent be thoroughly destroyed.—Eds.]

Recurrence of Nevi after Incomplete Removal. Robert J Schoenfeld and Hermann Pinkus[8] (Wayne State Univ) studied microscopic sections from 19 *cases of recurrent pigmentation* after cosmetic removal of a *mole* *In all cases* but 1 in which the original lesion was probably a wart lying near a junction nevus there were remnants of the original nevus present as nests of cells lying in the pars reticularis of the dermis (Fig 11) They showed no signs of activity and were covered with a layer of fibrous scar tissue The scar in turn, was covered with regenerated epidermis showing nests of nevus cells with varying amounts of pigmentation at the dermoepidermal junction *In 2 cases* in which specimens of the original lesions as well as of the recurrent ones were available, the former were mature intradermal nevi with a few cell nests still present at the junction In some of the sections in which there were remaining hair roots the source of the recurrent junction nevus was thought to be nevus cells around the hair root In other sections the junction

(8) A.M.A. Arch. Dermat. 78:30 33 July 1958

ing its high incidence in the yellow race. It is seen less often in Negroes and seldom reported in Caucasians. Nevertheless, the authors observed 7 cases within 2 months and believe that lack of recognition is the cause of its apparent rarity.

The typical clinical finding is cutaneous pigmentation accompanied by ocular pigmentation. Its tonality varies and sometimes is indefinite—a mixture of brown, blue and black—hence the designation "brownish blue." Cutaneous melanosis is usually unilateral, though sometimes bilateral, affecting preferentially the skin area corresponding to the 1st and 2d branches of the trigeminal, zygomatic and maxillary branches, a zone with a propensity for dysembryoplasias. The pigmented area may be more or less homogeneous, spotted or elevated; it may consist of small macules separated or arranged in a network of dark color which involves particularly the inferior lid and may include the upper lid, the frontoparietal region, and even the nose and mouth. On its surface are zones that resemble blue nevus clinically and histologically, thus showing the close relation between the two dermatoses. In some cases the pigmentation is found in the region of the mandibular nerve and in others follows the topography of cervical superior thoracic nerves. The deep situation of pigmented elements makes therapy ineffective. The lesion is benign, but 2 cases of malignant degeneration have been reported.

Ocular pigmentation is present in about 70% of cases. It appears as slate blue, round or irregular islets in the sclera. There may be heterochromia of the iris because of increased pigmentation on the affected side and also pigmentation of the conjunctiva or even of the cornea. Extension of ocular melanosis may produce a completely pigmented sclera. Hyperpigmentation of the fundus has been reported and in some cases melanocytic infiltration may affect the extrinsic ocular muscles, the retro-orbital fat and even the orbital periosteum.

Six of the authors' 7 patients were women. (In another series of 110 cases all but 22 were women.) In over 50% of the present series pigmentation, especially ocular, was noted at birth. In 1 the nasal lesion appeared at age 28 and in another at age 40. All patients were white except 1 who had a Negro great-grandmother. The lesion was unilateral in all. Deep ocular fundus lesions were not observed and hetero-

Such examination would allay any anxiety of the patient and permit recognition of the extremely rare nevus that shows histologic evidence of malignancy despite clinical quiescence as determined by an experienced dermatologist.

► [These findings fit in with those of Walton, Sage and Farber (A.M.A. Arch. Dermat. 76:193, 1957) who reported that junctional activity when present in rebiopsy specimens, was histopathologically similar to that in the first biopsy. The 112 rebiopsies reported by Walton *et al.* and the 19 histologic examinations in the report of Schoenfeld and Pinkus, of course, are not sufficient to prove that in an occasional case partial removal of a nevus with junctional elements may not cause activity. However, the 131 biopsies in these two studies speak against the likelihood that inadequate removal of junction nevi per se is sufficient to produce transition to malignancy of a previously benign lesion.—Eds.]

Junction Nevus with Spontaneous Clinical Disappearance. Max Braitman[9] (West New York, N. J.) reports a case.

White woman, 45, had a flat, hairless, pale brown plaque just below the hairline on the right side of the forehead. The oval lesion had a slightly elevated border, was about 1½×1 in. in size and had been present for many years. There had been recent increase in size. Biopsy showed considerable pigment in the lower rete and basal cell layer. Some of the cells were arranged in small groups. The corium showed no noteworthy change. Diagnosis was nevus pigmentosus (early changes of junction type).

The patient was seen by a group of dermatologists at a conference. The majority opinion was to do nothing except to watch and wait. The patient reported for examination at regular intervals for 1 year and then was not heard from until 7 years later, when she returned with dermatitis of the feet. Examination revealed no sign of the nevus. She stated that during the past few years the area had become progressively paler and flatter and had finally disappeared. There had been no treatment.

► [There is much evidence available at present which indicates that the junctional component of pigmented nevi undergo gradual change and diminish over a period of years. From adolescence to adulthood the junction nevus becomes a compound and finally an intradermal nevus. These histopathologic changes may account for the clinical differences in appearance of such lesions. Perhaps this mechanism is responsible for the spontaneous disappearance of occasional lesions.—Eds.]

Dermo-Ocular Melanocytosis (Nevus of Ota) belongs with blue nevus and Mongolian spot to the group of circumscribed congenital cutaneous melanoses characterized histologically by elongated fusiform melanogenic cells, classically considered to be of mesodermal origin according to Aaron Kaminsky, Jorge Daitsch and Jorge Abulafia[1] (Buenos Aires). This lesion was observed in 0.5% of all dermatologic patients at Tohoku University, Japan, during 1940-50, show

(9) A.M.A. Arch. Dermat. 77:721, June, 1958.
(1) Arch. argent. dermat. 7:231-241, September, 195

changes n Sutton s nevus, in which the nevus tissue is also phy iologically speaking at the periphery of the vitiligo Vitiligo as seen here is, therefore a more complex condi tion than vitiligo as ordinarily understood, in having both a biochemical and an anatomic substratum that affects many tissue mponents n the dermis.

► [Sutton referred to this nevus as leukoderma acquisitum centrifugum It has also been referred to as halo nevus and leukopigmentary nevus. —Ed.]

Centrofacial Neurodysraphic Lentiginosis, a congenital disorder characterized by lentiginous pigmentation across the nose and upper cheeks, neuropsychic changes and dys raphic manifestations, is described by A. Touraine[3] (Paris) on the basis of findings in 32 patients. Since he first described this condition in 1941 a few reports by other authors have appeared, but the cond tion has not recei ed widespread at tention and ha been ignored in recent textbooks on derma tology

Of the author s patients 17 were aged 8-15 11 were aged 17 28 and 4 were aged 30-40 The small pigmented spots, separated by healthy kin, are un formly brown have definite borders are flat or lightly elevated and are localized specificall the center of the fa e. The number of spots may ry from 15 to 200 mo w th the distribution somewhat butterfly haped In e epti nal cases, the spots may extend to the f ehead temples, el d cheeks nd chin. Two patients also had pigmented n o the neck and back, 2 had flat hemangioma (1 p houlder) nd 1 had warty hairy nevi on th loin and thigh According t the parents the facial pigmentati appea ed duri g the first months of life or toward the end f the 1 t ea The pigmentation increased sl wly until bout age 8-10 then tended to decrease or d sappea pontaneously The pigmentation was not affected b light and wa no more profuse in umme than in winter

Neuropsychic d sturbances wer present in 29 pat ents. Neurologic ymptoms, sometimes multiple were noted in 6 patient (1 had infantile hemiplegia, 3 had convulsions dur g ea ly infancy 4 had epileptif rm ttacks) Seven showed se ere mental retardation 7 showed definitely low intell gen e and 9 did poor work in school Others showed emo t onal n tabil ty temper tantrum social maladjustment,

[3] Presse méd. 66:16 1 1443 Oct 18, 1958

chromia of the iris was present in only 1 who also presented cutaneous lesions typical of blue nevus

Histology of Sutton's Nevus. Any process which makes a cellular nevus disappear is of theoretic interest and in Sutton's nevus this sometimes happens. Here, a vitiliginous condition not only sometimes depigments the centrally placed nevus but may bring about its destruction This morphologic change conflicts with the prevailing view of vitiligo as a purely biochemical lesion With these problems in mind, G. H Findlay[2] (Univ of Pretoria) studied 8 Sutton's nevi histologically In all cases, there was no other vitiligo apart from depigmentation around the nevus.

Where pigment was still present in the tissue it was largely of the chromatophore type of melanin in the papillary layer of the corium Only 2 of the specimens showed a well preserved and typical nevus structure, and in 1 of these the lesion was regarded as a blue nevus In the rest varying degrees of disarrangement had taken place

The nevus cells lost their identity mainly by coarse cytoplasmic vacuolation leading either to enlargement of the cell or to collapse and crowding of the cellular material in watery spaces Cellular disintegration took place by lysis or rhexis The nevus zone itself was invaded by cells of the lymphocyte-monocyte series which were often hard to distinguish from altered nevus cells Some monocytes appeared to arise by proliferation from adventitial germ centers All lesions in which cells were present were remarkable for their dense cellular packing with closed capillaries and no great intercellular edema or new fiber formation The process was sharply limited to a band of cells lying between the subpapillary layer and the upper corium above the sebaceous glands. No invasive features of deeper nevus extension were noted Fibroblastic replacement of the mass took place from below After disappearance of the cellular infiltrate the collapsed pigment free framework of the nevus consisted of a loose collagen network with some presumed increase of ground substance and dilated capillaries

The occasional case of vitiligo has been reported in which lymphoreticular proliferations have been present at the edge of the active zone. These would appear to stand closest to the

(2) Brit. J Dermat. 69:389-394, November 1957

sels, each lined with a single layer of endothelium and separated from each other and the epidermis by variable, usually ery thin, zones of connectiv tissue Treatment with repeated applications of solid car bon dioxide was not beneficial.

In most n tances of keratotic hemangioma, progressive development of hyperkeratosis has been noted after the ini tial angiomatous phase. The lower extremities have been i olved in all reported cases In Wertheim s opinion there s an actual ncrease in vascular elements n the area. Th s i



Fig. 12 (Courtesy of Laca, P. R. et al. A.M.A. Arch. Dermat. 73 215-31 February 1956.)

in contrast to the angiokeratoma described by Mibelli, in which the capillaries dilate. The vascular proliferation of hyperkeratotic angiomas s immediately under the epidermis, whereas in angiokeratoma of Mibelli a band of connective tissu separates the vessels from the epidermis. Angiokera tomas arise from preformed capillaries and are acquired le sion with a congenital predisposition but keratotic heman giomas are congenital in themselves.

The a thors believe that tissue asphyxia and possibly trau ma play a role in hyperkeratosis that develops in keratotic hema giomas.

defective memory etc Dysraphic manifestations were present in 15 patients In 8 patients 14 manifestations of anterior dysraphia occurred in 9 patients, 12 of posterior type and in 3 patients 3 of lateral type.

Coexistence of centrofacial lentiginosis and neuropsychic disorders was observed in 90.6% of the patients, skin pigmentation and dysraphia in 47 1% and all three signs in 40 6% These facts indicate that presence of these various signs in the same patient is not coincidental and that this triad constitutes a specific clinical entity Its mechanism is probably as follows dysraphia probably affects the base of the skull always accompanied by gliomatosis extending toward the encephalon which accounts for the neuropsychic disorders and toward the pituitary which accounts for the central facial pigmentation along with possibility of an adiposogenital syndrome

Heredity is an important factor in the etiology In the families of 22 of the 32 patients on whom family history was obtained, 38 instances of centrofacial lentiginosis were found. In 17 families in which examinations could be carried out, 32 persons had this pigmentation In 9 families the pigmentation was found in 1 parent and in 1 or several children indicating dominant hereditary transmission There is some evidence that syphilis may play a role in causing the mutation that leads to this neuroectodermosis.

► [Touraine states that this syndrome can be differentiated from the Jehgers Peutz syndrome in which similar pigmentations on the oral mucosa, lips, circumoral area and digits are associated with generalized intestinal polyposis —Eds]

Keratotic Hemangiomas. Philip R Loria Vincent J Derbes and John D Krafchuk[4] (New Orleans) were able to locate only 8 reported instances of keratotic hemangioma in ... Th y report 2 additional cases.

...ed verrucous lesions on the anterior ... They were elevated 3-4 mm. and in ... y adherent scales. Both lesions were ... ation. They had been of lifelong duration ... keratotic in the past 15 years. Biop... lomatous epiderm s above a diffuse ... r dermis. The epidermis showed ir... zone of hemang... regular areas of hyperplasia and atrophy with numerous finger-like acanthoses projecting into the dermis around hemangiomatous areas. The papillae and upper dermis conta ned numerous dilated blood ves-

(4) A.M.A Arch Dermat. 77 216-219 February 1958.

keratosis configuration in immediately adjacent areas and w th minimal inflammatory changes.

Likely many or most of the cases of supposed cancer aris ng in seborrheic keratoses reported in the literature, includ ng Sutton and Sutton s squamous cell keratoses were pseudoepitheliomatous hyperplasia (Weidman) in sebor rheic keratoses. No unequivocal evidence was found, either n a study of the present material or in a careful review of the l terature to indicate that seborrheic keratoses ever gi e rise to actual cancer

► [W agree with Row that in most cases the diagnosis of seborrheic keratosis can be made without error on clinical grounds alone When thi is not the case, caution should be exerted in the attempt to establish the diagnosis, before such lesions ar widely excised or deeply excavated on the basis of an erroneous clinical diagnosis of basal cell epithelioma, prickle cell epithelioma or malignant melanoma

W are not convinced that Row is correct in stating that seborrheic keratoses probably never gi rise to actual cancer Such an occurrence may be exceedingly rare but this does not mean that it never takes place W hav recently taken car of patient ith prickle cell epithelioma hich clinically seemed to arise from seborrheic keratosis The histopathologist, ho as not told of this particular feature, made diagnosis of keratosis, probably seborrheic keratosis with malignant changes!—Eds]

Multiple Keratoacanthoma Report of Extensive Case and Its Response to Therapy presented by Alfred J Ephraim and Jerom J Kaufman (Brooklyn)

Woman, 65 had about 20 dime-sized lesions on the left forearm 9 ears before. During the next year the lesions disappeared spontaneously lea ing flat atrophic scars. Fiv years later new lesions appeared on the left upper rm They were destroyed with the electric needle but new lesions appeared in some of the scars. N lesion disappeared spontaneously During the following 3 years lesions appeared on both forearms and arms.

Examination revealed round, elev ted, hyperkeratotic and verrucous lesions, rying in size from that of a dime to that of silver dollar The larger lesions were annula and crater-like with clea trophic white depressed centers Biopsy showed pronounced irregula acanthosis with no inv sion of the surrounding tissue Relatively mild, mostl peri ascular inflammatory reaction w present. The surface highly erroeou and covered with tremendously in sed and partl parakeratotic horny layer w th no sign of anaplasia

The patient treated with various sal es and lotions without sible change A course of cortisone gi en for arthritis produced no improvement. However after 6 intramuscula injections of bismuth subsalicylate some improvement noted After 15 njections there definite improvement, especiall of the larger lesions

► [The author refer to characteristic lesions of multiple keratoacan-

———— 34 Arch Dermat 77 91 94 February 958

Seborrheic Keratoses I "Pseudoepitheliomatous Hyperplasia" (Weldman) According to Lyon Rowe[1] (Los Angeles) a surprisingly large percentage of seborrheic keratoses subjected to microscopic study have been misdiagnosed clinically Among 244 such lesions the clinical diagnosis was seborrheic keratosis in 176 nevus in 40, verruca vulgaris in 13 basal cell carcinoma in 8 senile keratosis in 2, skin tag in 3 prickle cell carcinoma in 1 and melanoma versus nevus in 1 In most instances the microscopic appearance of the misdiagnosed lesions is sufficiently suggestive of the usual picture of seborrheic keratoses to give no further difficulty Occasionally however lesions clinically seborrheic keratoses, or resembling some other cutaneous entity show no resemblance to a seborrheic keratosis microscopically but rather closely resemble a prickle cell carcinoma with whorls, swirl and pearls of prickle cell Some of the lesions show typical seborrheic keratosis configuration in adjacent areas or in subsequent biopsies

Rowe followed 3 patients clinically and with repeat partial biopsies. Two had keratotic papular lesions with angiomatous elements similar to those seen in a case described by Weidman as seborrheic keratosis with pseudoepitheliomatous hyperplasia As in Weidman s case pearls and whorls were present in acanthomatous areas. In 1 of the 2 patients there was no change toward malignant appearance in a 3-month interval by the usual histopathologic standards. In the other the lesion showed reversion to a seborrheic keratosis with an inflammatory cellular infiltrate The third patient had a lesion clinically resembling a verrucous seborrheic keratosis or perhaps a senile keratosis From the microscopic sequence however the lesion started and ended as a serrated seborrheic keratosis of the type first described by Becker with one biopsy in between resembling the seborrheic keratosis with pseudoepitheliomatous hyperplasia Finally the lesion underwent complete involution leaving normal skin

In sections from the 244 lesions studied anaplasia whorl swirls and pearls of prickle cells were often found associated with marked inflammatory cell infiltrate in the cutis and edema and parakeratosis in the epidermis In 8 sections, areas of acanthomatous change were found with typical seborrheic

(1) J. Invest. Dermat. 29 165 189 September 1957

keratosis configuration in immediately adjacent areas and with minimal inflammatory changes.

Likely many or most of the cases of supposed cancer arising in seborrheic keratoses reported in the literature, includ ing Sutton and Sutton's squamous cell keratoses were pseudoepitheliomatous hyperplasia (Weidman) in seborrheic keratoses. No unequivocal evidence was found, either in a study of the present material or in a careful review of the literature, to indicate that seborrheic keratoses ever give rise to actual cancer

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We are not convinced that Rowe is correct in stating that seborrheic keratoses probably never give rise to actual cancer. Such an occurrence may be exceedingly rare but this does not mean that it never takes place. We have recently taken care of a patient with prickle cell epithelioma which clinically seemed to arise from a seborrheic keratosis. The histopathologist, who was not told of this particular feature, made a diagnosis of keratosis, probably seborrheic keratosis with malignant changes!—Eds.]

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Woman, 65, had about 20 dime-sized lesions on the left forearm 9 years before. During the next year the lesions disappeared spontaneously, leaving flat atrophic scars. Five years later new lesions appeared on the left upper arm. They were destroyed with the electric needle but new lesions appeared in some of the scars. No lesion disappeared spontaneously. During the following 3 years lesions appeared on both forearms and arms.

Examination revealed round, elevated, hyperkeratotic and verrucous lesions, varying in size from that of a dime to that of a silver dollar. The larger lesions were annular and crater-like with clear atrophic white depressed centers. Biopsy showed pronounced irregular acanthosis with no invasion of the surrounding tissue. Relatively mild, mostly perivascular inflammatory reaction was present. The surface was highly verrucous and covered with a tremendously increased and partly parakeratotic horny layer with no sign of anaplasia.

The patient was treated with various salves and lotions without visible change. A course of cortisone given for arthritis produced no improvement. However after 6 intramuscular injections of bismuth subsalicylate some improvement was noted. After 15 injections there was definite improvement, especially of the larger lesions.

► [The authors refer to characteristic lesions of multiple keratoacan-

thoma. Judging from the photographs of the lesions in the original article, they are not convincingly those of keratoacanthomas. They appear to be quite verrucous and present different shapes and bizarre border outlines; central horny plugs are to a large degree missing and only flat atrophic scars remain after their spontaneous disappearance. Even the course and the histopathologic picture are not typical for this entity.—Eds.]

Epithelioma Spinocellulare Segregans: So-called Adenoacanthoma of Sweat Glands (Lever). J. Delacretaz, A. S. Madjedi and R. M. Loretan[7] (Lausanne) report 15 cases in which the histologic changes described previously by Lever as adenoacanthoma of the sweat glands were observed. The

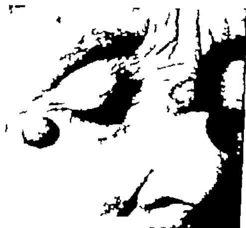


Fig. 13.—Local recurrence of tumor and skin metastases 1 year after treatment. (Courtesy of Delacretaz, J., et al.: Hautarzt 8:512-518, November, 1957.)

patients (9 men and 6 women) ranged in age from 61 to 90 (average 75). The size of the tumors varied, and the period of time until therapy was started ranged from 2 months to 10 years. The clinical appearance varied also: ulceration was noted in 7 patients, a keratotic or verrucous surface in 3 and a nodular surface in 3. No pertinent data were available on 2. Local recurrence and skin metastases were observed (Fig. 13). In 10 patients multiple epitheliomas or precancerous foci coexisted. Lethal metastases occurred in 2 patients.

Histologically, there was *neoplastic proliferation* of the prickle cell type. The cells showed a particular generalized tendency to individual keratinization and segregation (through loss of intercellular connections). The separated cells became necrotic. Subsequently cavities developed that

(7) Hautarzt 8:512-518, November, 1957.

contained granular cell residues. The cavities were often surrounded by a single cell layer which gave them a glandular appearance. The glandular character of the tumor may be apparent early when a tubular mass develops, or it may develop late, when cavities form progressively in the tumor. Both types of development may be present in the same tumor.

In none of the 15 patients were the authors able to prove a relation between the sweat glands and the tumors. Therefore, the authors doubt the origin of adenoacanthomas from sweat gland canals as claimed by Lever. They consider them to be tumors of prickle cells and propose to call them epithelioma spinocellulare segregans.

Relationship between Bäfverstedt's Benign Lymphadenosis of Skin and Jessner's Lymphocytic Infiltration of Skin. C. Postma and J. Th. F. Sluiter[3] (Univ. of Amsterdam) report a case corresponding clinically with Jessner's lymphocytic infiltration, but histologically resembling benign nonfollicular lymphadenosis of the skin.

Woman, 34, had recurrence of skin eruption 20 times in 5 years. At intervals of several weeks to several months, one to four small round, flat papules or nodules appeared on the eyelids, behind the ears or on the arms. The size was usually that of a pea or bean, but a few times lesions about cm. in diameter occurred on the legs. Sometimes the nodules had narrow elevated margin and sunken center or were annular. Color ried from that of normal skin to slightly reddish. The lesions disappeared spontaneously after a few weeks or months. The general examination and blood picture were normal. In histologic preparations, hyperplastic lymphatic tissue was found repeatedly. There were no follicles. The histologic picture remained unchanged and did not suggest a systemic affection. The impression was that of lymphoreticular hyperplasia without follicular structure or reaction centers.

Under the term "lymphocytic infiltration of the skin," Jessner and Kanof described a series of patients with recurrent papular lesions similar to those observed in the authors' patient. Histologically there were sharply demarcated lymphocytic foci embedded in a fine reticulum in the cutis. Although Jessner, Calnan and others believe that these so-called lymphocytic infiltrations are not related to benign lymphadenosis of the skin (Bäfverstedt) and do not resemble it, the present authors after careful study of the literature and prolonged observation of their patient, conclude that Jessner's lymphocytic infiltration is not an independent path

[3] Acta dermat.-venereol. 33: 98-194, 1953.

ologic picture but a variety of benign lymphadenosis of the skin In most if not all patients with benign lymphadenosis of the skin the disease can be recognized histologically and distinguished from lymphatic leukemia.

► [It would be a step backward to consider lymphocytic infiltration (Jessner) and benign lymphadenosis as being identical. Lymphocytic infiltration occurs on the face, chest and arms, but neither Jessner nor we have observed it on the earlobes a typical localization of benign lymphadenosis The lymphocytic foci are not deep in the cutis and there is no tendency to the formation of the typical germinal centers of lymphocytomas Lymphocytic infiltration often responds to chloroquine and other antimalarial drugs, but we know of no reports of such a response in lymphadenosis benigna.—Eds]

Reticulohistiocytoma (Reticulohistiocytic Granuloma) is a seldom recognized but serious condition of unknown cause involving the skin often with destructive changes in the joints bones and synovial membranes accompanied by histiocytic reactions. Lesions in the skin precede the destructive changes in the joints synovial membranes and bones.

Hamilton Montgomery Howard F Polley and David G. Pugh[9] (Mayo Clinic and Found) report 2 cases.

Case 1.—Woman, 24 had nonerythematous, grouped, translucent discrete, flesh colored to brownish round to oval papules and nodules on the face, sternum, arms (Fig 14) and fingers (Fig 15) Severe, destructive progressive arthritis roentgenologically and clinically differing from psoriatic or rheumatoid arthritis, was present. Biopsy of a skin lesion showed large and giant histiocytes and no definite deposition of lipids. In time the skin lesions involuted, but arthritis became extremely severe and disabling

Case 2.—Woman 59 had several soft purple raised nodules on dorsum of fingers, hands and right elbow and severe destructive arthritis of the hands A specimen from the dorsum of the right forefinger revealed the typical histologic picture of reticulohistiocytoma. A synovial biopsy showed large histiocytes similar to those present in the skin A similar picture was found in the bone Reactions to periodic acid Schiff and sudan black B stain were greater in the bone and synovium than in the skin (Fig 16) suggesting the presence of lipofuscin. This however may have been a degenerative phenomenon and not a primary factor

Reticulohistiocytoma is not due to a disturbance in lipid metabolism in the sense that the condition can be regarded as one of the xanthomatoses The positive reaction to sudan black B explains the faint reaction encountered with sudan IV stain in the second patient and in other cases in the literature.

As in the first patient cutaneous lesions in the second pa

(9) A.M.A. Arch Dermat 77 61 72, January 1958



Fig (above left) — Translucent papules on arm of woman, 2

Fig 15 (above) — Characteristic changes in cutaneous nodules on fingers in same patient.

Fig 16 (left) — Section from cutaneous lesion in woman, 59, showing weakly positive PAS reaction in histiocytic giant cells, reduced from 155

(Courtesy of Montgomery H et al A.M.A. Arch Dermat 77 6 72, January 1958)

tient m olnted whereas arthritic symptom and destructi e bon changes progressed. Why n some patients the d sease ho ld m ol te spontaneously after mild arthr tic changes and n others progres t mutilati g and destructiv changes m the joint and bones emain to be d termi ed.

Clinical Picture of Destructi e Joint Changes with Multiple Reticulohistocytoma of Skin s described by D lia Walth (Uni of Frankf rt) with eport of a case Skin hang h cutaneous and subcutaneou nodes ha e long been bserved in rheumat c d seases For the past 20 ear ne ther elat ely rare disease seen w th a serious ften d tructi bone and joi t d sease has created wide interest I most tances t ha been ferred to as reticuloh t c toma

All eported pat ent p esented l anced, sometimes mu-

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tilating joint changes and skin manifestations. The latter consisted of yellowish to brown red papules and nodules, pinhead to pea sized located usually on the backs of the fingers and hands joints ears head, cheeks near the nose and the neck and shoulders Similar nodes were observed on the tendon sheaths and mucous membranes The skin lesions preceded often by many years the joint lesions and later regressed spontaneously often to complete disappearance while the destructive joint changes progressed. Histologically granulomas were observed in the skin which contained round cells some neutrophils eosinophils histiocytic elements and many giant cells with 1 20 nuclei and eosinophilic homogeneous or slightly foamy plasma In the differential diagnosis xanthoma histiocytoma and granular cell myoblastoma were considered

Woman, 38, had migrating rheumatic involvement of almost all joints with gradual stiffening of both hips. The skin changes preceded the rheumatic involvement by several years and began with skin-colored or slightly yellowish red papules on the forehead and lateral parts of the face accompanied by itching When the lesions on the face disappeared, papules up to lentil size appeared on the shoulders anterior aspect of the trunk inner and extensor surfaces of the thighs and legs. There were a few papules on the back of the right wrist and 3 papules on the back of the left hand.

Within 1 year biopsy specimen were taken of 5 similar papules and examined histologically Four specimens revealed several granulomas, partly in the cutis and partly in the subepidermis. The epidermis appeared acanthotic and the subepidermal cutis edematous and partly metachromatic Sudan III staining revealed fat droplets in numerous cells. The granulomas were surrounded by a network of thin connective tissue fibers and separated by dense bundles of collagen tissues. There was cellular infiltration around the small vessels, which showed thickened walls with large swollen endothelial cells often projecting into the lumen In all specimens, the granulomas consisted of the same cell types Besides varying number of neutrophils and eosinophils there were fibrocytes and fibroblasts, which often had pale, bizarre nuclei and there were some large histiocytic elements which usually had 1 2 pale nuclei with vacuoles or honeycomb structure. Further giant cells with dark nuclei rich in chromatin occurred in varying numbers, occasionally simulating Sternberg's giant cells.

The author considers the reticulohistiocytomas a manifestations of a granulomatous allergic reaction in the course of rheumatic disease

Dyshidrosiform Eruptions and Sweat Organ I Morphologic Findings in Six Patients with Hyperhidrosis and Vesicular Eruptions of Palms and/or Soles. Franz Herrmann, Soura D Morrill and Marion B Sulzberger[21] (New York Univ Post-Grad. Med School and Skin and Cancer Unit) in est gated the pos bility of whethe dyshidrosiform eruptions are ever d rectly related to the eccrine excretory ducts and whether hyperhidrosis play a decis e role in the pathogene- of these eruptions

Biopsy pecimens of fresh skin lesions of 6 patients with hyperhidrosi and typ cal dyshidros form eruptions (cheiropompho) of the palms and/o soles were studied in serial section The e cision had to be made laterally close to the dorsal surface because the great number of sweat gland ducts would otherwise have made d fficult an accurate assessment f the fi d gs

In ? patients a direct connection was found between the lumen of the weat gland duct and cavity of the bl ster 1 of them presented th typ cal hist pathologic findi g of mili aria rubra These bservations imply that hyperhidrosis is the primary f ctor all these hanges. It seem to lead primaril t ncreased hydration and saturation with water of the basal c rneal layer e f the stratum compactum Pre umabl th welling could cause intra orneal obstruction f th cr tory d cts of the weat gla d lead g to tagna tio d pa age f weat and to the development of miliaria l k lesion and the absorption of transepidermal water (insen bl per piration) which normally takes pla e in the l wer trat m corneum, becomes more difficult. The impai ed d nage lead to blister formation n the epiderm s.

Nosographic Position of Sneddon-Wilkinson Disease among Primary Bullous Dermatoses was studied by Vitton Mesumeci (L of Catania) on the basis of typical cl n cal d h tologic find ngs 3 patients. Differential diagnosis w poss bl from dermatitis herpetiform s herpes gesta t m pu tula bacterid, pemphigus vulgaris of the bullous

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variety and Senear Usher pemphigus. Although the clinical aspects suggested the possibility of Duhring's disease the latter was excluded by the histologic finding of a subcorneal bulla which is the distinctive feature in Sneddon Wilkinson disease The author questions the validity of the accepted concept of the subepidermal localization of the vesicopustular lesion in Duhring Brocq disease and advances the hypothesis that the lesion may have a subcorneal localization in this condition also

A brief review of the literature indicates that several author (Civatte Cerutti) have suggested the possibility of a subcorneal localization of the lesion in Duhring Brocq disease Musemeci followed patients with this condition for several years. Histologic studies indicated that when several lesions from various areas were examined subcorneal masses were often present and some were so large as to be true bullae In other instances the subcorneal and subepidermal bullae coexisted or were superimposed His studies confirm the coexistence of dermoepidermic lesions with subcorneal bullae in Duhring Brocq disease which Sneddon and Wilkinson believe to be strictly connected with the disease that they separated and called an entity Sneddon Wilkinson disease should not be considered a new condition and an autonomous entity but only a form of Duhring Brocq disease

Subcorneal Pustular Dermatosis (Sneddon Wilkinson) M Doglioti (Univ of Turin) reports a case

Man, 36, had dermatitis of 2 years duration localized only in the area between the femoral condylus and the external malleolus of the left leg Morphologically the condition showed elements that were first bullous and later pustular The dermatitis was subacute afebrile and without itching characterized by periods of recovery that alternated with periods of exacerbation, without evident cause and without sequelae except for moderate residual hyperpigmentation The lesions tended to heal in the center and progress peripherally with a small edge The patient's general condition was not impaired. Histology showed subcorneal bulla formation filled with lymphocytes rare eosinophils and detritus of fibrin. No etiologic agent was ascertained. Prednisone combined with wide-spectrum antibiotics brought about recovery in 15 days. Earlier therapy with sulfonamides by other physicians had caused violent urticaria like reaction on large part of the skin.

Clinical and histologic findings were in every respect those described by Sneddon and Wilkinson and the author l a l n

(4) Minerva dermat. 33 73-6, March, 1958

lifficulty in establishing the diagnosis. The only new feature was the mode of therapy This condition should be considered a clinical entity completely separate from those that ha e milar morphologic aspects. Although Duhring Brocq lisease shows objective nd subjective find ng commo to subcorneal pustular d rmat tis, the histologic fin ling of a *ubcorneal bulla, which has been described in all cases of* th latter condition reported so far i only a ca ual finding i Duhring Brocq disease.

Subcorneal Pustular Dermatosis. Charles H Breenbaum nd James B Lee[3] (Pennsylvania Hosp Philadelphia) report case corresponding in the sal ent features with those of S eddon and Wilkinson.

Woman, 68 w ho-pitalized for skin eruption of 3 year dura tion, neck pain and general red muscle weakness. Abnormal physical findings w re limited to the skin nd mucous membranes. There were grouped esicles and pu tules arranged over the abdomen, buttocks nd lower back girdle-l ke fashion and grouped lesions in the axillae and inframammary areas. The early lesions were pinhead-sized esicles arranged in groups, w th a surrounding rea of ery thema Pustules of the same ze were present, some w th umbilicated enter There were also many hyperpigmented areas on the skin of the bdomen nd axillae and 2 bluish esicles i the oral cavity Part l healed carbuncles were ituated at the right lumb ne posteriorly nd at the right upper sternum

A biopsy specimen of the skin showed superficial subcorneal esi cle containing neutrophil and protein precipitate w th neutrophil extension to the derm and neighboring epidermis. There was m ld spongiosi of the epiderm and mild perivascular lymphocytic and plasma ell infiltration of the corium.

With 1 Gm chloramphenicol daily and warm saline soaks the ca buncles healed rapidly and completely Coincidentally there was resolution of the esicular and pustular eruption. N new lesions appeared after eeks treatment. Because of a toxic neutropenia, chloramphenicol was stopped after 1. days, and 1 Gm. novobiocin daily wa started The patient w discharged improved 2. day fter admission

Subcorneal pu tular dermatos i a d sease seen mostl n *middle-aged* women, haracteri ed by terile pu tules and cles occurring in groups and singly with a predilection f th xillae, girdle region and flexor areas Patients are go d general health, with little or no discomfort. The pustules are filled with neutrophils nd debris Whether subcorneal pu tular *dermatosis i* a separate entity or an

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variety and Senear Usher pemphigus. Although the clinical aspects suggested the possibility of Duhring's disease the latter was excluded by the histologic finding of a subcorneal bulla, which is the distinctive feature in Sneddon Wilkinson disease. The author questions the validity of the accepted concept of the subepidermal localization of the vesicopustular lesion in Duhring Brocq disease and advances the hypothesis that the lesion may have a subcorneal localization in this condition also.

A brief review of the literature indicates that several authors (Civatte Cerutti) have suggested the possibility of a subcorneal localization of the lesion in Duhring Brocq disease. Musemeci followed patients with this condition for several years. Histologic studies indicated that when several lesions from various areas were examined subcorneal masses were often present and some were so large as to be true bullae. In other instances the subcorneal and subepidermal bullae coexisted or were superimposed. His studies confirm the coexistence of dermoepidermic lesions with subcorneal bullae in Duhring Brocq disease which Sneddon and Wilkinson believe to be strictly connected with the disease that they separated and called an entity. Sneddon Wilkinson disease should not be considered a new condition and an autonomous entity but only a form of Duhring Brocq disease.

Subcorneal Pustular Dermatosis (Sneddon Wilkinson)

M Dogliotti[4] (Univ of Turin) reports a case

Man, 36 had dermatitis of 2½ years duration localized in the area between the femoral condylus and the external malleolus of the left leg. Morphologically the condition showed elements that were first bullous and later pustular. The dermatitis was subacute afebrile and without itching characterized by periods of recovery that alternated with periods of exacerbation, without evident cause and without sequelae except for moderate residual hyperpigmentation. The lesions tended to heal in the center and progress peripherally with a small edge. The patient's general condition was not impaired. Histology showed subcorneal bulla formation filled with lymphocytes, rare eosinophils and detritus of fibrin. No etiologic agent was ascertained. Prednisone combined with wide-spectrum antibiotics brought about recovery in 15 days. Earlier therapy with sulfonamides by other physicians had caused violent urticaria like reaction on large part of the skin.

Clinical and histologic findings were in every respect those described by Sneddon and Wilkinson and the author had no

(4) Minerva dermat. 33 73-76 March, 1958.



Fig. [illegible] Subcorneal pustular dermatosis in Negress, 25. Note general configuration and distribution of lesions and tendency to extend from intertriginous areas, forming fairly large plaques with narrow vesicopustular borders. Face and lower parts of extremities are essentially clear. Three years later plaques were smaller (some over [illegible] cm.) and serpiginous feature was missing. (Courtesy of Ellis, F. A.: A.M.A. Arch. Derm. 78:[illegible], November 1958.)

penicillin and tetracycline as does impetigo. The vesicles of dermatitis herpetiformis, erythema multiforme and bullous pemphigoid are characteristically subepidermal and can be readily distinguished from the subcorneal vesicles.*

* In some cases of pemphigus the vesicle or bulla is interpreted to be subepidermal instead of intraepidermal. In some cases of dermatitis herpetiformis perhaps the vesicle or bulla forms subcorneally or intraepidermally instead of subepidermally.

uncommon variant of dermatitis herpetiformis is unknown. If they are the same disease the present concept of the histologic characteristics of dermatitis herpetiformis will have to be revised.

Subcorneal Pustular Dermatosis is a term used to describe patients with clinical features that are almost identical with *dermatitis herpetiformis* but in which the subcorneal vesicles are virtually indistinguishable from those of impetigo. Frances A. Ellis[6] (Johns Hopkins Univ.) reports 3 cases and reviews data on 11 cases in the literature. The characteristics of these 14 cases are remarkably constant and much like those originally reported by Sneddon and Wilkinson.

The disorder is encountered primarily in women over age 40. It is characterized by superficial vesicopustules which form annular or gyrate plaques with irregular spreading borders (Fig. 17). The lesions are located primarily on the torso and upper parts of the extremities involving the intertriginous areas about the breasts, axillae and groin. The lesions involute to form thin superficial crusts followed by residual hyperpigmentation without atrophy. The lesions recur in overlapping waves of healing and persist over a number of years. Local and systemic antibiotics are not helpful but in general response is achieved after therapy with sulfapyridine or one of the sulfones.

The histologic features include a subcorneal vesicle varying in size from 0.1 to several millimeters in diameter. The vesicle is covered by a thin keratin layer with the base formed by the granular layer containing a thin layer of frankly purulent material that consists of serum, leukocytes and leukocytic debris with an occasional acantholytic cell in the base of the blister. The rete may be normal or slightly acanthotic and show minimal edema and exocytosis. The papillary and subpapillary layers may be involved with light edema and mild round cell infiltrate.

The clinical course in subcorneal pustular dermatosis is clearly distinguishable from that of impetigo. The disorder appears in an older age group than is usual in impetigo, the vesicles often are sterile and distribution and size of the vesicles is far more extensive than in impetigo. Subcorneal pustular dermatosis is not contagious and does not respond to

(6) A.M.A. Arch. Dermat. 78:580-583, November, 1958.

corneal pustular dermato is reported by Sneddon and W l kinson Characteristics of the new syndrome were described a (1) rythematopu tular eruptio of chron c progres ion (2) ma ntenance of general health (3) characteristic h tologic p ctur nd (4) response to diaminod phenyl lf me therapy Review of the l terature o thi yndrome d on impetigo herpetif rmis (known f r 70 years) along w th tud f 3 patient persuaded the authors that t liffi ult t nd iduahze a new syndrome among acute and chron current pu tula lermatoses Conf ion exi ting with regard to th three principal type pu tular psoria i acro-lermat tis cont ua and impetigo herpetif rmis, m y be dis-pated onl by accurat etiologi information or by e hans t tud f large series f cases. Until knowledge of these n l tion more c mplete the general term recurrent pu t loses is preferred for all patient i whom more spe-n diagnos q estionabl

Cas 1—Woman, 39 had chronic pustula eruption for 12 years, hich had been interrupted by many acute episodes, t first accompanied by mild fever Exacerbation f cutaneou lesion occurred predominantl during premenstrual periods. The patient also had lesions of the scalp, ey brows, buccal mucosa and nails. I some at tack cutaneous lesions wer accompanied by nodular lesions on the leg which might be diagnosed a nodula sculitis.

s —Man, 45 had cutaneous lesion similar to those of the l ent in C se 1 hich had progressed for 15 y ars. At first, the erupt on ma hav been eczematiform, but at time of examination the eruption were definitely pustular High fever accompanied one of these attack

s 3—Man, 40 had eruption of 6 months duration similar to that the patient in C ses 1 and 2 Besides cutaneous ymptoms, hairy egions ere invol ed, along w th xillary and posterior cervical adenopathy H had several ch lls, but never had checked the temper ature Great improvement occurred with use of diaminodiphenylsulfone 50 mg day th practical cure occurring w thin 3 weeks

The patient C ses 1 a d 3 howed clinical ign f 7 m ne gen ral ed phthos Bes les th nodula and m u membra lesio the patient n C se 1 both had lesions n hairy reas, and the patient in Case 3 also had mall pu t form sca a l locall at m f les n in sebor he region

Criteria for Histopathologic Diagnosis of Dermatitis Herpetiformis (Duhring's Disease) and Erythema Multiforme. l l era d Ad Dupont nd A Fontai e[5] tudied the lesion

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Arch belges dermat et syph 326 1955, December 1955

Dermatitis herpetiformis, subcorneal pustular dermatosis of Sneddon and Wilkinson, and some cases of grouped pustular eruptions of the palms and soles have in common a favorable response to sulfapyridine and certain other sulfonamides and sulfones. Perhaps this common response is due to the fact that these three dermatoses are variants of the same disease process. —Eds.]

Subcorneal Pustular Dermatosis. Report of Case is presented by *Robert J. Schoenfeld*[7] (Wayne State Univ.)

Woman, 63, Negro, had recurrent generalized skin eruption of 20 years' duration. The abdomen, scalp, distal parts of extensor surfaces of the upper extremities and most of the lower extremities were covered with superficial, flaccid, fragile, dome-shaped bullae 0.5-1 cm. in diameter and filled with turbid fluid. Many of the lesions had opened, dried and were exfoliating, but no denuded areas were present. There was hyperpigmentation at sites of previous lesions. Nikolsky sign was absent and there were no oral or anogenital lesions. Acute exacerbations lasting 10-14 days alternated with longer periods in which the eruption was chronic and less extensive. Biopsy of a lesion on the arm showed acanthosis of the epidermis. The stratum corneum was lifted off; the space beneath it was filled with coagulated serum and leukocytes. No micro-organisms were noted. Some leukocytes and eosinophils were noted migrating through the epidermis, which was not particularly edematous and showed no acantholysis. There were some leukocytes in and around blood vessels in the cutis, but no other remarkable evidence of inflammation.

[illegible] a regimen of $KMnO_4$ baths, chlor[illegible] [illegible] and diphenhydramine hydrochlo[illegible] [illegible] weeks later slight exacerbation [illegible] therapy, but a few lesions continued to form at irregular intervals. The lesions disappeared for several weeks while treatment with prednisolone, 5 mg. 3 times daily, was given. Therapy with sulfapyridine, 0.5 Gm. 3 times daily, produced a remission for 2 months.

The lesions of subcorneal pustular dermatosis are extremely superficial vesicles that proceed to superficial scaling. They may or may not show grouping, often affecting the extremities, but may be generalized. The lesions tend to recur, though response to treatment is prompt and remissions may last months. They resolve with hyperpigmentation and are extremely pruritic. General health is not affected. Histologically, the *bulla is like that of impetigo contagiosa*, but it is sterile. Until more cases can be studied the disease should be considered an entity separate from dermatitis herpetiformis, which it resembles in many ways.

Recurrent Pustuloses were studied by [illegible] and J. Pinol Aguadé[8] (Barcelona, Spain) with reference to the sub-

(7) A.M.A. Arch. Dermat. [illegible]
(8) Presse méd. 66: 1491-1499, Oct. 1, 1958.

ariably levated in patients with pemphigus as compared w th norm l ubjects. Pla ma fibrinolys n tends to be higher n the presenc f increased numbers of crusted and/or bullo lesion n the kin In bullous diseases, there is some dence of an in erse ratio between activator and plasma fibrinoly i levels. There is no apparent correlation betw een nh b t r and fibri lysin le els in the patient with pem phigu or n control groups

The a thors believe that the increase n proteolyt c ac t t in patients with pemph gu primary in the kin rathe tha in the plasma. The low bluster threshold in these patient may ind cate that th skin is lready the site of in creased proteolyti acti ty M reover a low bluster threshold wa bserved in an area of localized (vulvar) pemphigus sociated with a normal bluster threshold in a distant ite, gge t ng a local cutaneou rather than a systemic origin f r the nc eased proteolytic acti ty If this is the case th crease n pla ma fibrinoly in observed in patients with pemphigu may e lt from absorption of skin protease into the pla ma. Present method f identification of pla ma fi brinol do not ex lude poss ble ugmentati n from cu ta e u bsorption

Adrenocortical Dysfunction in Early Stage of Pemphigus Vulgaris. H \ Cohen T D Ullmann and A Dostro ky[2] (Hebr w U H da sah Med School) studied 13 patients w th pemph gu ulgari and 14 control subject ncluding 8 w th derm t t herpetiform s. Patient with pemph gus ll had the d sease in its earl stag with only a few k n or muc m membrane lesion Diagnos n all patient w th bullou rupt o was based on h tologic examination of at lea t tw d fferent l ions. The following test were per f rmed t luat drenocortical function (1) salt toler test bef and fter adm n tration of 10 mg des y rt steron etat (2) R binson P ower nd Kepler test 3 Thorn 4-hour ACTH test d (4) 24-hour xcretion of l k t ster id in the rin

It w ll k own that the alt tentio ca sed by desox rt costeron tate pronoun ed in patient with defin te l nocortical n uff cienc and those w th the linical fea f Addison d sease But, n patient with only light

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layer was broken in many areas presenting lakes of pus. The same lesions were found on the scalp. The nails also were involved.

Histologic examination showed huge intracorneal pustules with extremely acanthotic epidermis. The epithelial cells were disrupted by edema and migrating cells. In the upper cutis around the vessels was an infiltrate consisting of macrophages, lymphocytes and cells with segmented nuclei. The vessels contained many eosinophils. The entrance to the follicles contained large parakeratotic horny masses. In other sections, normal keratin layers alternated with pustules.

Serum calcium was 6.4 and 7.6 mg./100 ml. (normal 9-11 mg./100 ml.). Eosinophilia was 12-20%. The pustule content grew staphylococci. On A.T. 10 (total 32 cc.) and calcium tablets, the lesions subsided within 3 weeks and the serum calcium level became normal. Histologic studies after 14 days of A.T. 10 treatment revealed heavy parakeratotic partly basophil horny layers covering a moderately acanthotic epidermis. The papillary vessels were extremely dilated. Around the superficial vessels, especially in the subpapillary layer there was minimal lymphocytic histiocytic infiltration.

About 18 months later, after febrile tonsillitis, tetanic attacks recurred accompanied by pustules on the trunk and limbs. On vitamin D_2 and calcium tablets, the skin lesions regressed within 3 weeks.

The healing stage was similar morphologically to psoriasis and could not be distinguished from it histologically. There are, however, certain differences between the two entities. Impetigo herpetiformis develops only in hypocalcemia which is the sequela of parathyroid hormone deficiency or due to disturbances in calcium metabolism during pregnancy. Lack of calcium appears to be the cause of impetigo herpetiformis because it promptly subsides on A.T. 10. These characteristics distinguish impetigo herpetiformis from psoriasis vulgaris, pustular psoriasis and from Hallopeau acrodermatitis as an independent entity.

► [Apparently there is no uniformity in the finding of hypoparathyroidism in all cases diagnosed as impetigo herpetiformis. The therapeutic effectiveness of A.T. 10 (tachysterol, dihydrotachysterol) in some cases is well known. Other forms of therapy including ACTH and corticosteroids have been reported as effective. Among the many interesting features of this case are the resemblance to psoriasis in the healing phase and the 12-20% blood eosinophilia.—Ed.]

Proteolytic Activity in Pemphigus. II. Estimations in Skin and Blood. John W. Dougherty, Frank E. Cormia and Shirley Unrau[2] (Cornell Univ.) found that a hemorrhagic vesicle can be produced regularly in human skin by intradermal injection of the proteolytic enzyme trypsin. In most patients with pemphigus vulgaris a definite reduction in blister thresholds is found. Plasma fibrinolysin (or protease) ...

[2] A.M.A. Arch. Derm. 77:281-284, March

F entually the conjuncti al sac is closed completely an l the e eball immobilized. The scar tissue presses on the lacrimal ducts causing the conjunctiva and the cornea to dry

L ually other mucous membranes also become invol ed, particularly those of the oral cavity nasopharynx, larynx d anogenital regions. In more advanced cases the mucosa f the esophagus and even the lower parts of the alimentary tract may be invol ed Vesicles nd bullae appear on the mu cosae wh ch break easily leaving eros ons. A characteristic feature hrinking and atrophy of th mucous membranes.



[illegible] ocular changes typical of so-called pemphigus ocularis. Extensive con[illegible] tissue proliferation. (Courtesy of Jablonska, S. et al. Acta derm.-venereol. [illegible] 37

I about half the cases blist r ppear o the kin They uall ha e a thick, fa rly strong roof occur on unchanged k n nd n some cases lead to scarring

Th autho describe a cli call ty p cal case of so-called pemphigu ocularis nvolving the conjuncti a (F g 19) and the mucosa f th mouth nasoj harynx, lar x and gen talia. I th l sease cc se th r were l so som recurrent bullous le m th k F r comparison a case f early pemphi gu lgari d ing the conjuncti a and oral nd nal mucosa lescribed Diagnos wa establ hed in the early t ges f the d sease by cytologic exam nation of mear from the mucos Lat a t p cal bullou eru pt on ppeared on the k

I true pemphigu cytologic xamination reveal the pres en f ca tholytic ell which predominat over nflam

adrenocortical deficiency a considerable spread in the result and overlapping with the findings in normal subjects may be assumed Thus a clearcut distinction between entirely normal subjects and patients with only slight dysfunction of the adrenal cortex can hardly be made on the basis of the results of tests similar to that used in this investigation. Therefore it is of interest that whereas patients with Duhring's disease and other skin conditions showed decreases as well as increases in water and salt excretion after desoxycorticosterone acetate resulting in an average decrease of about 29% for sodium for the whole group none of those with pemphigus showed any increase in water and salt excretion and the average decrease in excretion of sodium was 49% This difference is not statistically significant because of the great personal variations but it appears of sufficient interest to warrant further investigation

The results of the other three procedures showed no evidence of adrenocortical dysfunction in the control subjects, but some of the test results suggested adrenocortical dysfunction in the pemphigus patients

Deviations from normal in water and salt metabolism as suggested by this study may be a side effect of some other adrenocortical dysfunction which may be etiologically connected with pemphigus and which should be sought by other procedures such as hormone assays

► [Although the difference might not be statistically significant, the fact that the findings in pemphigus differ from the other bullous diseases tabled makes them worthy of consideration. Perhaps there is some adrenocortical dysfunction associated with pemphigus vulgaris —F. J.]

Pemphigoid Mucosae So-called Pemphigus Ocularis and Its Relation to Pemphigus According to Stefania Jablonska, Pawel Segal, Boguslaw Milewski and Halina Dabrowska[4] (Warsaw Med School) the name pemphigus ocularis is inconsistent with the fact that the disease is not a true pemphigus. It is a distinct entity which on clinical, histologic and cytologic grounds belongs in the group of pemphigoid. The most characteristic clinical changes are those involving the eye. Initially there is *a catarrhal conjunctivitis* with a ropy mucoid discharge. Subsequently scarring thickening and shrinkage of the conjunctiva appear with adhesions running from the bulbar conjunctiva to the eyelids (Fig 19)

(4) Acta dermat. -venereol 37 364-375 1957

Of 25,000 consecutive patients with skin diseases 1,625 (6.5%) had psoriasis and 133 (0.53%) had persistent pustular eruptions of the extremities (44 of these were males). Of the 1,625 with psoriasis 35 (2%) had pustular eruptions of the extremities. In 3 patients pustular psoriasis occurred in a generalized form and proved fatal after many years.

The author presents excellent photographs of the three variants of chronic pustular eruption of the palms and soles in the original article.

► [It is unfortunate that so little is known about the etiologic mechanism of these persistent pustular eruptions of the hands and feet. We have not been impressed by the role of foci of infection. It is not clear to us why involvement of the palms and soles suggests probable emotional instability. In some cases the systemic administration of the newer sulfonamides and antibiotics, especially of the newer prednisolone analogues such as triamcinolone, appears to be helpful. We agree with Ingram, however, that topical therapy particularly with tar and dioxyanthranol (anthralin, cignolin) is the treatment of choice.—Eds.]

Prospect of Psoriasis. Of 918 patients with psoriasis seen during the past 5 years, Ronald Church[8] (Royal Infirm, Sheffield, England) interviewed 540 and reviewed their histories. Age at onset was predominantly 5-15 years. Most severe cases began in early childhood. A family history was obtained in 34% of the patients. Of 116 with severe psoriasis 41.5% had a family history of the disease.

Nearly half of 37 patients who were first seen for guttate psoriasis had had a recurrence. In 50% of these an attack of tonsillitis was recorded as the precipitating cause. The total incidence of rheumatoid and psoriatic arthritis was 2%, which is less than the 3.1% found in the general population. Pregnancy and parturition had no effect on the disease course in 14% of patients; 33% became free from psoriasis and in 11% the disease became worse. In 44% parturition was accompanied by relapse of psoriasis, whether it had cleared during pregnancy or not.

In 400 patients the disease had been present long enough to judge its course before treatment. Of these 74% had never been free from psoriasis. Of those who had had remission most had been free for only 6-12 months. Only 8% had been clear for 5 years or more.

The response of 200 patients to treatment with tar baths and ultraviolet was good. The lesions cleared completely in

[8] Brit. J. Dermat. 70: 39, 1958, April, 1958.

matory cells in the smear The presence of a single acantholytic cell is without significance. In pemphigoid eruptions, the cytologic picture is dominated by many inflammatory elements accompanied by more or less numerous epithelial cells which may be edematous or show other changes but no distinct acantholysis The name pemphigoid mucosae is suggested for so-called pemphigus ocularis

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7 PSORIASIS

Pustular Psoriasis John T Ingram[3] (Univ of Leeds) considers acrodermatitis continua or perstans pustular psoriasis and pustular bacterid to be variants of one distinctive clinical entity or one particular pattern of reaction. Since these affections are four times commoner in psoriatic *patients than in others he prefers the label pustular psoriasis* to cover the whole group The eruptions appear to be combinations of eczematous and psoriatic reactions and like so many combinations owe their recalcitrance to that fact

The real cause of these reactions is not known though infection trauma or toxic or emotional stress may act as precipitating factor Histology does not help in interpretation and does not *differentiate the three types of reactions.* The presence or absence of staphylococci in the lakes of pus is not significant The site of election the anatomic and physiologic skin peculiar to palms and soles must be significant and suggest physiologic probably emotional instability But general measures of treatment such as antibiotics sedatives and steroid hormones are without effect

As with most reactions in *which the epidermal component* is significant topical measures are the more valuable in treatment though radiotherapy is of no value Tar and a sulfonated bitumen preparation resembling ichthammol (ichthyol) or combinations of these may be beneficial but do not readily clear the affection

(3) A.M A. Arch. Derma 77 314 318 Mar ch 1958

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The real cause of these reactions is not known, though infection, trauma or toxic or emotional stress may act as precipitating factors. Histology does not help in interpretation and does not differentiate the three types of reaction. The presence or absence of staphylococci in the lakes of pus is not significant. The sites of election, the anatomic and physiologic skin peculiar to palms and soles, must be significant and suggests physiologic, probably emotional, instability. But general measures of treatment such as antibiotics, sedatives and steroid hormones are without effect.

As with most reactions in which the epidermal component is significant, topical measures are the more valuable in treatment, though radiotherapy is of no value. Tar and a sulfonated bitumen preparation resembling ichthammol (ichthyol) or combinations of these may be beneficial but do not readily clear the affection.

(5) A.M.A. Arch. Dermat. [illegible]

entir thickness of the nail resembling the nail of a seam stress. Similar erosions may be seen in patients with eczema or other dermatoses and also in generalized diseases wh ch affect the trophi m f the nail but these are much more su perficial, do not contain friable material are often more ir regular and prob ng does not cause pain as in true psoria i These nonspecific lesions may be present also in a pat ent w th psoriasis, but i s ch cases, are not man festation of true ungual psoria but of a trophi d turbance due to local or generalized disease

The proces of formation of psoriatic erosions i of diag nostic mportance these are formed i the zone of the ungual matrix and result from a true psoriatic invol ement of the matrix visible i the portion f the na l occupied b the lunula. It is a tru psoriatic papule which begin in the epidermal layer of the matrix, leading to softening of horn ti sue of the lamina with a proces analogous to that of cutaneous para keratosi and n the derma, to secondary reactions of cap l laries. Th rosions, thus formed, proceed with d tal growth of the nail toward th free edge.

The psoriatic pap le may also form bungally and is revealed as red points, corresponding to d lated capillaries seen through the na l, which retains t smooth normal sur face Occasionall a matrical erosion, with growth of the nail corresponds t ubungual papule giving the impres sio f softening and erosion through the nail but ord narily the subungual lesion does not rise through the nail.

Nardell suggests n explanation for the different response of nail and f ha to psoria s. The nail s a product of the epid rmi and participates with the rest of the skin in epi dermal function and it di turbance by disease wherea hai is subject to the determining and dom nant influence of the dermal papilla and remai unaffected b the psoriatic proc ess wh h is essentially ectodermal

Etiology and Pathogenesis of Psoriasis Vulgaris are dis cussed by N Melczer and J Bodzay (Univ of Pécs) The observation that the Kobner phenomenon a part of col loidopexy and identical w th the t rage of electronegati e v tal benzidine tains the area of skin irritations, opened new avenues in the tudy f the pathogenesis of psoria is

(1) [illegible] 9 31 331, August, 938

95 (37%) and improved greatly in 141 (54%). Most patients, however, had remissions lasting no longer than 6 months and 11.5% of those who cleared completely relapsed in 4 weeks.

The younger the age of onset and the more numerous the other affected members of the family, the more severe and persistent the disease is likely to be. Much can be done to alleviate or even clear the eruption with intensive light therapy, but its effects are temporary and freedom from the disease for 5 or more years is unusual. In young patients with extensive psoriasis the disturbance caused to their mode of life justifies recommending a change to a sunnier climate.

► [The 2% incidence of arthritis in this series should be correlated with the age of the patients at the time they were examined. It appears possible that had the author compared those of his psoriasis patients who were aged 40 or over with patients in the same age group but having nonpsoriatic eruptions such as lichen planus, dermatitis herpetiformis and other dermatoses, he would have found a significantly higher incidence of arthritis among the patients with psoriasis.—Eds.]

Nail Changes in Psoriasis, according to Leonardo Nardelli (Rome)[7] are of two types: (1) true ungual psoriasis with specific manifestations of this disease and (2) nonspecific atypical changes secondary to psoriasis or its complications, similar to onychoses of other origins.

True psoriasis of the nails is not often the only manifestation, conversely, cases are not rare in which at the beginning of a recurrence after complete regression or at onset of extension of a discrete stationary dermatosis ungual changes may be the only manifestation; this is followed by other cutaneous manifestations. In these cases localized recurrences tend to repeat themselves in the form of the previous attack. Sometimes the patient himself discovers that changes in the nails are the first sign of an approaching recurrence. More often ungual psoriasis accompanies cutaneous lesions throughout their course and appearance of a normal ungual lamina marks the beginning of remission. The normal nail appears in the proximal portion with a smooth lunula and proceeds to grow distally. The border between psoriatic and normal nail is arched anteriorly (semilunar curve of the psoriatic nail). The most characteristic aspect of true ungual psoriasis is a punctate onychia. The ungual lamina presents a variable number of points of rounded erosionimplying the

(7) Gior. ital. dermat. 99: 257-268, 1958.

ted in areas where moi ture had appeared. The erythem deepened in intensity fo several hours then gradually faded over sev ral days a the lesions healed. In lesions destined to show a Kobner reaction variabl number of erythema tou papules persisted and acquired a recognizable psoriatic scale afte 14 days. Persi tent erythema and positi e Kobne reaction were not observed in areas where stripping had t pped bort of producing vis ble moisture.

On the ba of thi study it appear that trauma l m ted t uperficial ves els with xtravasation of blood cells and pla ma i not ufficient to cau e th Kobner reaction in psoria i Neither i stripping of th uperficial layers of the tratum corneum sufficient It not known whether epider mal damage a essential in p oducing the Kobner reaction by means of mechanical trauma, because vascular reactions alwa s f llowed epidermal njury Further investigations h uld be mad to d termine whether capillary inflammation n tself can cause the Kobner reaction

* (Undoubtedly the cause of the Kobner phenomenon in psoriasis is more than the stimulation of epidermal or dermal structures the degree of trauma must also play role —Ed.)

Psoriatic Arthritis and Elevated Erythrocyte Sedimentation Rate. Most textbooks stres the d fficulty of d fferentiat ing psoriatic and rheumato d arthriti Several dist ngui h ng teat res ha been described Psoriatic arth opath i sa d t h w predilection for j nt of the term nal pha la ges wherea rheumatoid arthritis sel l m in olves these j nt k se agglutination reaction u ually absent in pso t arthriti and present i rheumato d arthritis Some author ha eported that the x ray appearance in psoriat c rthriti haracterist and completely unl k that seen in heumat d arthrit Ma ked levation of the erythrocyte sed ment ti n rate i considered typical of rheumatoid d se but re rtedl t ly moderat l levated psori t arthrit

\ t sh H Gent l B Lagerholm and \ Karlstr k rolm ka Hosp Stockholm) eport that the sedimenta t markedly elevated (er 100 mm) n 25% of patient w th psoriatic arthrit treated during th pa t ear Tw c ses are reported, the diagnosis in both bei g borne out by the bsenc f carditi rheumat c nodules pre

(1) Acta dermat venereol 37 459 464 957

vulgaris Since the Kobner phenomenon correspond to pexis all diseases presenting this phenomenon which have various etiologies but a common pathogenesis can be grouped under the heading of pexidermas or pexismoses. Thus psoriasis vulgaris is considered as a storage disease a pexiderma or pexismosis

The total fat content of the psoriatic scales is about 1.8 time greater than that of the psoriatic papules This means about 100% increase in the fat content of the scales, considering the approximate 40% water loss which normally occur in the horny layer

In the psoriasis factitia focus the lipids accumulate in the endothelial cells of the capillaries of the superficial vascular layer as well as around them Of the lipids derived from psoriatic scales only the phospholipids caused late inflammation when injected intracutaneously into patients with psoriasis and into healthy persons Cholesterol cholin and neutral fat were ineffective The causative phospholipid is probably lecithin

The clinical sign of psoriasis such as hyperemia infiltration and later parakeratosis are probably related to a disturbed fat metabolism of the skin caused by stored histamine-like tissue substances which liberate various inflammatory lipids

Vascular Trauma and Pathogenesis of Köbner Reaction in Psoriasis Richard P Reinertson (Nat l Inst of Health) injured the uninvolved skin of 20 patient with psoriasis in three ways (1) suction until confluent petechiae formed, (2) scarification with production of superficial bleeding and (3) removal of layer of stratum corneum with cellophane tape to about the level of the granular layer or upper malpighian layer with appearance of a moist surface A Köbner reaction followed scarification in 7 cases and cellophane tape stripping in 8. None of the 20 patient had a reaction in site of superficial petechiae Most patient with reaction had eruptive or widespread lesion

Effect of cellophane stripping were not limited to the epidermis. Shortly after the procedure localized erythema and sometimes a surrounding flare and wheal appeared. The wheal and flare lasted only a few minutes but erythema per

(9) J Invest Dermat. 30 283 284, June 1958

ted in area where moi ture had appeared The erythema deepened i 1 tenaity f r several hours then gradually fa led several days a the le ions healed. In lesions destined t show a Kobner reaction, variable numbers of erythematous papules persisted and acquired a recogn zable psoriatic scale after 14 days. Persistent erythema and po itive K b-ner eaction were not observed in areas where stripping had u pped hort of producing visible moisture.

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Psoriatic Arthritis and Elevated Erythrocyte Sedimentation Rate Most textbook t es the d fficulty of differentiat ng ps riatic and rheumatoid arthriti Se eral d tingui h g feat re hav been described Psoriatic arthropathy sa d t how pred lection for joint of the terminal pha l g h rea rh umatoi l arthritis seldom n ol es thes j t R se agglutinat on reaction u ually absent n psori t c rthriti and present n heumat d arthritis. Some uthor ha e reported that the x ra appe rance n psoriatic rthriti haracteristi nd completely unlike that seen in heumato d rthrit Ma ked elevation of the erythrocyte sedim ntat rat i con idered typical of rheumatoid di se but eportedly t onl mod rat l l vated n psori t rthrit

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1) Acta dermat venereol 37 44 444, 57

vious infections erythema nodosum and leukocytosis and the presence of normal titers negative Rose agglutination reactions and predilection of the joint disease for the terminal phalangeal joints Electrophoretic analysis however disclosed moderately elevated alpha₂ and beta globulin fractions such as is observed in rheumatoid arthritis. In both patients the skin changes and joint involvement became worse during steroid therapy This response by the joint disease is particularly interesting because steroid therapy usually is highly beneficial in rheumatoid arthritis

► [As far as we have been able to tell the arthritis in our psoriasis patients responded very well to systemic corticosteroid therapy —Eds]

Studies on Serum Lipids Proteins and Lipoproteins in Psoriasis. Walker A Lea Jr Herbert H Cornish and Walter D Block[2] (Univ of Michigan) studied 18 patients aged 23-55 with active psoriasis and 10 normal control subjects. In 4 of the psoriatics the total lipids cholesterol and phospholipids were elevated One other patient had a slightly elevated total cholesterol Although some variation from normal was found in the serum protein pattern of the patients with psoriasis there was no consistency with respect to the protein fraction affected Results of lipoprotein analyses (in 9 cases) indicated abnormalities in the *S 70-400 fraction* in 6 cases in the *S 40-70 fraction* in 5 in the *S 25-40 fraction* in 2 in the *S 20-25 fraction* in 2 and in the *S 1 10 fraction* in 2

Though some abnormalities were obtained in the determinations carried out in this study they were not striking The data might be interpreted to indicate that total lipid and/or total cholesterol were elevated in a significant number of psoriatics However if the lipid data are considered in connection with the serum protein and lipoprotein data and with the clinical findings a different interpretation is presented Thus the elevated lipid fractions in 5 patients with psoriasis were accompanied by an elevated beta globulin beta lipoprotein or both These changes considered together are consistent with results obtained in atherosclerotic patients If the data are further correlated with the clinical findings in the 5 patients relative to atherosclerosis diagnosis of latent or overt atherosclerosis can be substantiated in

(2) J Invest. Dermat 30 181 185 April, 195

ea h Ther f e all the lipid elevation observed in thi gr oup of 18 patient with psoriasi might be accounted for on the ba i of cl cal find ngs relative to atherosclerosis The find g n th investigation yield no evidence to indicate that psoria accompan ed by abnormal erum lipid level

Serum Lipoproteins in Psoriasis E lward M Shapiro J h M Kno and Scott Grundy (Baylor Uni) carried ut serum lipop tein and serum cholesterol determinatı n 9 men d 10 women with psoria l The patient were not n pecial l ets nor were they receiv ng any y tem c medicatio f treatment of their psoria ı The serum l po pr tein w re naly ed by ultracentrifuge u ing the method described b Gofman and associates The serum chole terol alue w re mea red b the method f Pearson Stern and McGa ck

Re ult of th tudy re ealed no ncrease in lipopr tein lev l f eith the Standard S_f 0-1 or S_f 12-400 values The mea lues for these le l were l ghtly low a c om pared t the ge er l population The serum cholesterol al ues f m n w re normal howe er th y were slightly le- ted f w men

Metabolic Studies in Psoriasis Skin Potassium and Plasma Potassium, Chloride and Alkaline Values during Clinical Improvement. A Rei berg J Bourgeois-Spina se, M H k and F Sid (Pari) found kin potassium levels were normal n th un nvolved kin and very high in the le ion of 70 psoriat c patient Th d tu bance decreased when linical impro ement occurred under treatment Pla ma pota um sod um chloride and alkali e reserve were nor mal duri g th act ve phase of psoriasi During impro ement ther w a loweri g f pl sma pota sium in 31 of 44 patients a lowering f pla ma hlorid in 16 of 23 and an ease of lkal ne eserv 10 f 16 Th changes were tat t call gn ficant although th alues remained within ph iologicall no mal limit Pla ma sodium and glucose d d not ry ignificantly during l nical mpro ement In ll cases h cal mprovement wa obta ed through ener g ti top cal therapy Internal therapy produced pott d rregula es lts

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(2) J Invest. Dermat. 30 181 185 April, 1958

psoriatic skin. However this as well as the other biochemical disturbance described for psoriatic plaques in recent years appear to be consequences of the disease rather than part of the basic causal mechanism.—Eds.]

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8. LUPUS ERYTHEMATOSUS DERMATOMYOSITIS SCLERODERMA

Critique of Concept of Pre-L.E. Cell. During the past years, Frances Pascher and Alexander Horota (New York Univ. Post-Grad. Med. School and Skin and Cancer Unit) examined more than 1,500 samples of peripheral blood for the presence of L.E. cell by the technics of Haserick, Math M ffatt Barnes o Magath. Specimens were drawn from 750 patient with diverse cutaneous and visceral disorders and from 11 healthy vol nteers. Cell resembl ng the so-called pre L.E. form were found not only in systemic lupus erythemat sus but also n localized and systemic condit on in taneou nd isceral d seases, n association with negati e w ll posit ve L.E. test and in the normal subject. The highest ncidence 9-10 of these forms/500 normal leukocytes occurred n cases of rheumatoid arthriti and in 1 f chron c d sco d l pu erythematosu. The a erage number was /500 leukocytes.

Th utho con der these cell to be decomposition form because of their strik g resemblanc to decomposition form (Abbauf rmen)described some years ago n the course of in vitro studies of c llula disi tegratio in peripheral blood w thout relation to the L.E. phenomenon. A number of out ta ding hemat logi t concurred that these form were ar tefa t ttributabl to degeneration. Attention called to th fact that there ample t me f decomposition to set in during the cou se of making an L.E. preparation ince the phenomenon requ es at least ½ hour nd, a a rule 2 or more hours f opt mal development.

Th intensely basophilic dense, homogen ed nu lear ma t rial f decomposition forms appear different from the mu h less compact pale-stai ing nuclear material which make p the nclusion body of the L.E. cell. Cytochemical tudies also indicat that the two may be di tinct. Because f

Blood 11:376-381, April, 1956.

The accumulation of potassium in lesions of psoriasis is probably due to acanthosis and the abundance of young epidermal cells. It is known that any active cellular proliferation is accompanied by an increase in potassium content. In this sense the accumulation of potassium cannot be considered specific for psoriasis. But since it is generally accepted that potassium is indispensable to the anabolism of protein and carbohydrates and hence to the cell structure, it is conceivable that it plays an important role in the psoriatic lesion. It is possible that by diminishing the potassium content of psoriatic lesions their proliferating capacity may be decreased like that of any other tissue rich in potassium.

The egress of potassium ions from cells can be related to an increase in hydrogen ions in these cells, whatever the cause for this increase in hydrogen ions may be (glycolysis, direct corticosteroid action, etc.). Therefore the clinical improvement observed in patients with psoriasis may be the result, among others, of a gain in hydrogen ions and a loss in potassium ions of the involved tissues. The fact that the topically active substances in psoriasis for the most part are strong reducing agents (tars, oil of cade, chrysarobin, anthrarobin, etc.) and certain topically applied acids may be cited in support of this hypothesis. Thus the humoral changes found during clinical improvement in psoriasis could result from the local treatment and the skin changes. It is well known that hypopotassemia associated with hypochloremia and alkalosis may be associated with loss of potassium ions and gain of hydrogen ions by the tissues.

A second hypothesis should be considered, viz., that the cutaneous changes are the result of primary humoral change. The tendency toward hypopotassemia and alkalosis suggests the possibility of an increased adrenocortical secretion, particularly aldosterone. If true, sodium retention and eventually weight gain and increased blood pressure should be observed. None of the patients in the present series showed these symptoms. Furthermore attempts at treatment by parenteral corticosteroids or ACTH failed in most of them. Aldosterone levels were not determined in these patients and it is not known whether an increased secretion of this hormone is or is not present.

► [Another interesting biochemical difference between psoriatic and n

ables i ol ed i leukocyte mobility chemotaxi an I phagocytosis

► [It ould be interesting to know the causal drug and the ariety of allergic drug eruptions in the 2 patient out of 11 ho had a positive reaction. The only drug hitherto generally accepted as producing a y temic lupu erythematosus-like yndrome i hydralazine hydrochloride (Apresoline) although similar eruptions due t hydantoin derivatives have recently been eported (see p 180) —Eds.]

Evaluation of Simple Precipitation Test for Systemic Lupus Erythematosus. An unusual precipitate observed during the determ nation of serum cholesterol in a patient who later showed ev dence of disseminated lupu erythemato u led Kenneth K. J nes a d H rry F Th mpson[1] (Tucson Ariz) t the elaboration f a test for this d sea e

Method.—Serum or pla ma, 0.1 ml i placed in a test tube and ml of 1% p-toluenesulfonic acid glacial acet c acid is pipetted dow the ide of the tube The tube is shaken allowed to stand 20 minutes, then reshaken If no clot or precipitate seen or if it d sappear on shaking the reaction is negative. If a precipitate persist 20 minutes after shaking and standing and then disappears on reshaking the reaction 1+ If precipitate persists after eshaking and standing 20 minutes, the eaction 2+ If the precipitate i heavy the reaction 3+ and if it ppears glas y gel the reaction is 4+

Of 13 patient acutely ill w th sy tem c lupu er thematosu 1 hibited test react on of 2-4+ nd 1 howed a 1+ rea tic Of 17 lupu erythematos n pat ent who wer in l nn l em whose d sease wa controlled by th rap 11 howed negati reaction and 6 showed 1+ Patient who ema ed se er ly ll h wed cont nuou ly elevated test es lt Those who esponded to therapy exhibited a fall t 1+ or egati test res lts. The reaction became m re po i t wh n xacerbation occurred.

Th test w egativ 134 f 142 patients with collagen d sease ther than y temi lupus and rheumatic disea e h w th h omi heumatoid arthriti and 1 with juvenile heumatoid rthrit gave 1+ reactions, whereas 1 w th h m rheumato d and 1 with ju n le rheumatoid arthritis ga e eaction The test was egati e in 64 patient w th mon diseases including syph lis, tuberculosis, heart d sease carcinoma and allergic dermatitis, d it was ega t 65 of 66 apparently healthy person One ga e a 1+ ea tion A false positive reaction was obtained 4 patient w th hepatitis (3-4+) 1 with iral hepatiti (1+) 1 with

[1] J.A.M.A. 44: 134-1438 Mar 22 1 B

these morphologic and histochemical differences it is felt that these nonspecific forms cannot be regarded as precursors of the L.E. cell These cells appear to have no diagnostic significance

Interaction of Nuclei and Globulin from Lupus Erythematosus Serum Demonstrated with Fluorescent Antibody Using the fluorescent antibody technic, George J Friou, Stuart C Finch and Katherine D Detre[6] (Yale Univ) demonstrated a globulin component with a marked affinity for nuclei in serum of patients with disseminated lupus erythematosus. The factor reacts with nuclei of most tissues of many vertebrate species When serum specimens are tested simultaneously against human tissues and material from other sources there is no apparent difference in brightness of the reaction indicating lack of any species specificity

Positive results were obtained with serum from 27 of 28 patients with disseminated lupus In many of these (including the 1 with negative serum) the disease was in a quiescent stage Only 9 gave positive L.E tests although the L.E. test had been positive in all cases at some time in the past. There was some variation from serum to serum in the intensity of the staining and this was consistent in repeated tests. Detailed analysis could not be made of the strength of the reaction in relation to disease activity but those patients with severe active disease tended to have most marked nuclear staining and those in partial or complete remission the least.

Positive reactions were observed in a few patients with disease syndromes known to be closely allied with lupus (rheumatoid arthritis scleroderma and dermatomyositis) and in 2 of 11 patients with allergic drug reactions Reaction in patients who did not have lupus erythematosus were relatively weak. No reaction occurred with the serums of 44 patients with various acute and chronic disorders other than those mentioned. Included in this group were serums which contained C reactive protein and heterophil antibody as well as those with various general alterations in protein fractions The authors suggest that the L.E. phenomenon requires participation of the factor demonstrated in this study plus vari

(6) J Immunol 80 324-329 April, 1958.

The pos bility that the L.E. factor i a ba ic protein can not be excluded. Howe er the following characteri tic would put the L.E. factor mor nto the group of ant bod es (1) Cell uclei, loaded w th the I F factor are ngested by granulocytes. (2) An experimental antinuclei serum how hara terist cs very simila to those of the I E. serum. (3) The ntigenic specificity for nuclei depend on the presenc of nucleoproteins

Latex Agglutination Test for Disseminated Lupus Ery thematosus is described by Charles L. Christian Ricardo Mendez Bryan and Daniel C. Larson (Columbia Univ.) Se rums were obta ned from 24 patient with documented dis- seminated l pu erythematosus, 6 with probable di semi nated lupu erythematosu 4 with discoi l lupu erythemato- us, 53 with heumatoid arthrit and 84 with a variety of di gnoses. Using a mod fication of the F II latex fixation test pol tyrene latex part cles (diameter 0.81μ) were coated w th calf thymu ucleoprotein Latex particles so treated were agglutinated by 19 of the 24 serums of pat ent w th documented d sem nated lupu erythematosu Agglutina tio w pos t e w th 2 of (serum of patient with probable disseminated l pu and wa negati e w th all serum of pa tient w th rheum t d arthriti and m scellaneous diseases.

Aggl t nation f nu leoprotei latex ppeared to be spe- ific fo di seminated l pu erythematosus. The test corre- lated losely with results f I E cell preparations on the sam serum Of particula nterest re th con istently neg ati e es lts w th rheumat id rthriti serum since the inci dence of pos ti e L F ell t t n these patients remains highl controver ial

Desoxyribonu leic cid mall mount inhibited nu leo- protei latex agglut ation. Absorption of d seminated lu pu ery thematosus serum with nucleoprotein latex remo ed the agglutination property and the L.F cell facto Present data suggest that the serum f ctor wh ch induces L.F cell formation is the sam that which aggl tinates nu leopro- tei latex particles and that th f ctor rea t primarily with des xyribonucleic acid

Some properties of the L.E. ell fact r ggest that it may be part of an mmunologic reaction with pecificit f nu

9) Proc. Soc. Exper. Biol. & Med. 98 : 820, Aug.-Sept. 1958

disseminated coccidioidomycosis (4+) 2 with fulminating *multiple myeloma (4+)* and 3 of 11 with discoid lupus erythematosus (1+)

The precipitation test seems to differentiate systemic lupus erythematosus *from periarteritis nodosa scleroderma,* dermatomyositis and rheumatic fever and gives few false positive reactions in rheumatoid arthritis The test result can be modified to some degree e.g. by therapy with adrenocortical steroids or corticotropin or by a remission but it appear to parallel the progress of the disease The identity of the substance causing the precipitation is obscure.

► [The value of this test for lupus erythematosus seems doubtful Lee and Schultz (J A M A 167 1552, July 19 1958) after using this test came to the conclusion that it "defines a non specific imbalance among the serum globulins and that "its specificity and sensitivity are not great enough to warrant its use as a routine diagnostic method in the disease DuBois, Rosenfeld and Ohtomo (J A M A 158 813 Oct 11 1958) came to the conclusion that the "test is completely nonspecific and that as a diagnostic procedure for systemic lupus erythematosus it should be abandoned. —Eds]

Serology of L.E. Phenomenon is discussed by P Miescher[8] (Univ of Basel) Because the L.E. factor can be adsorbed to specific cell nuclei it became possible to detect the factor with antiglobulin consumption tests. The principle of these tests is that the L E factor a gamma globulin can be taken up by cell nuclei and then liberated at 60 C The presence of the L E. factor in the eluate may be demonstrated by the fact that an anti human globulin serum can be partially neutralized in its activity by addition of the eluate Cell nuclei can be loaded with the eluate However the eluate is usually too weak for demonstration of the L E phenomenon

Using the antiglobulin consumption test the author found that the L.E. factor reacts specifically with cell nuclei and independently of the organ or species from which the nuclei were isolated (absent organ or species specificity) It was also observed that the L.E serum can be partially or completely inactivated by saturation with nucleoprotein or desoxyribonucleic acid

The author was able to demonstrate the L E factor by passive hemagglutination *when nucleoprotein or desoxyribonucleic* acid was used as an antigen However this test is less sensitive than the antiglobulin consumption test

(8) *Hautarzt 8 502-503, November 1957*

left eye. Electrophoresis showed decreased serum albumin (36.2%), considerable increase of gamma globulins (44.3%) with 7.2% beta, 5.1% alpha$_2$ and 7.2% alpha$_1$. Decrease of beta globulins was greater than usually seen in active lupus. Antierythrocytic antibodies (before transfusions) were strongly positive, especially autoagglutination of the patient's red cell (Coombs direct positive with 2 serums of different origin); agglutination of red cells sensitized by patient's serum in hyperalbuminous solution with red cell treated by papaine; cold agglutinins to human red cell were positive in 1:64 dilution. Consumption of antiglobulin of red cells sensitized by patient's serum was 100% and complement was decreased to 29 units (control 50). Leukoprecipitins gave only very weakly positive results.

The patient insisted on leaving the hospital when red cells had increased to 3,500,000 with 5,800 white cells. She remained on cortancyl, 60-80 mg./day for another month, during which temperature remained normal and hemogram was unchanged, reticulocytes being reduced to 5%. However the skin lesions over the ankles and tibial crests and the joint symptoms recurred.

It is interesting that in this case the formation of Hargraves cells was particularly active at the time of active hemolysis and the presence of antibodies in the serum. Whether the two phenomena are identical is a matter for future study.

Hepatitis and Cirrhosis in Women with Positive Clot Tests for Lupus Erythematosus. Lloyd G. Bartholomew, Albert B. Hagedorn, James C. Cain and Archie H. Baggenstoss (Mayo Clin. and Found.) report 7 cases. All 7 patients were females; 4 were under age 25. For periods of 6 months to 13 years before evidence of hepatic disease appeared, these patients presented protean symptoms consistent with the clinical diagnosis of disseminated lupus erythematosus. Episodic and migratory joint manifestations, including pain, swelling and redness, were prominent in 5 patients; the other 2 had significant arthralgia. Recurring unexplained fever was recorded in 6 patients. Typical pleuritic pain occurred in 4. Repeated examination of the urine in 6 of the 7 patients showed sporadic occurrence of albuminuria, microscopic hematuria and cylindruria. Five were sensitive to light or unusually susceptible to drugs. Intermittent, transient erythematous or urticarial eruptions were noted in 3 patients during an exacerbation of joint pains. All 7 patients had anemia. Although none gave a history of syphilis, a positive serologic reaction for syphilis was obtained in 4. Episodes of

(2) New England J. Med. 259:947-56, Nov. 13, 1958.

clear constituents At present this remains speculative and there is no evidence that the factor is responsible for the diverse manifestations of disseminated lupus erythematosus.

Lupus Erythematosus Disseminatus and Acquired Hemolytic Anemia with Autoantibodies were observed in a patient by Jacques Debray and Y. Najean[1] (Paris)

Woman 28, with a history of a rheumatic condition was hospitalized in April 1955 because of dyspnea on exertion and subfebrile asthenia which had been progressing steadily for several months She was extremely pale had a temperature around 100.4 F joint pain, a slight systolic murmur and moderate splenomegaly Red cell count was 1,500,000 with 350 000 platelets, 8,600 leukocytes and 50% polynuclear cells Serum bilirubin (80 mg.) was almost completely of indirect type Blood smears showed 27% reticulocytes and sternal myelogram contained 61% ... non rate was ... eral ... am ... strep- ... nemia were positive (Coombs direct, autoagglutination of red cell in protein saturation, autoagglutination of trypsinized red cell) Numerous Hargraves cells were found in the blood and marrow

Cortisone (300 mg./day) reduced the temperature and some ... later the joint swelling Red cell increased to 2 600 000 early in May when her husband insisted on her leaving the hospital prematurely She continued with the same dose of cortisone and red cells had increased to 3,200 000 by June 1 Antistreptolysin was reduced to 640 unit and other hematologic test though still positive showed improvement After sudden cessation of cortisone at the beginning of July red cell fell to ... 000 000 and test for hemolysis were again strongly positive She was seen briefly a few times during the following year and test showed progression of the syndrome Cortisone was taken irregularly and the patient husband refused to allow her to remain in the hospital for study Eventually she returned, very ill, in June 1957 Temperature had increased to 10... 104 F and dyspnea and pallor were extreme The joint had remained silent spleen was not enlarged and facial skin was normal There was no traumatic or infectious or drug factor to explain the sudden decrease in red cell to 600 000 with 12,600 white cell 69% polynuclear cell ...% myelocytes 89% reticulocytes and 1,700 000 platelet There ... a erythroblastosis of the marrow (60%) urobilinuria (but bilirubinemia did not exceed 10 mg.) and hemoglobin was 20 mg/100 ml Supplementary studies were made during emergency treatment (200 cc of deplasmatized red cells daily with 60 mg metacortandracin

The ocular fundus showed whitish exudate in the temporal region of the right eye and temporal punctate hemorrhages with cotton wool exudate and small exudates and hemorrhages in the nasal area of the

(1) Presse méd. 66 723-725 Apr 23 1958.

left e). Electrophoresis showed decreased serum albumin (36.2%), considerable increase of gamma globulins (44.3%) with 2% beta, 5.1% alpha$_1$ and 2% alpha. Decrease of beta globulins was greater than usually seen in active lupus. Antierythrocytic antibodies (before transfusions) were strongly positive, especially autoagglutination of the patient red cells (Coombs direct positive with 2 serums of different origin); agglutination of red cells sensitized by patient serum in a hyperalbuminous solution with red cell treated by papaine; cold agglutinins to human red cells were positi in 1:64 dilution. Consumption of antiglobulin of red cells sensitized by patient's serum as 100% and complement was decreased to 29 units (control 50). Leukoprecipitins ga only very weakly positive results.

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(2) New England J. Med. 259 947 56, Nov. 3, 1

unexplained weakness and excessive fatigability occurred in all

The recent development of jaundice or some other evidence of hepatic decompensation seemed to precipitate the terminal phase in the 4 patients who died of their systemic illness While at rest the patients had a good appetite were well nourished and showed a sense of well being belying the seriousness of their disease Spider angiomas were universally present and an easily demonstrable hepatosplenomegaly was present in most Among tests of hepatic function that gave unequivocally abnormal results were the thymol turbidity and cephalin cholesterol flocculation and determinations of serum albumin prothrombin time and serum bilirubin In all 7 patients marked hypergammaglobulinemia and extreme elevation of the sedimentation rate were present, and typical cells of disseminated lupus erythematosus were repeatedly shown in the serum and bone marrow

In view of the protean nature of disseminated lupus erythematosus and its characteristic involvement of the endothelium of small blood vessels it would seem strange if it did not at times involve the vast capillary network of the liver That such involvement actually occurs is suggested by the fact that the lymphatic vessels at the hilus of the liver are dilated and increased in a number of patients with disseminated lupus erythematosus even when there is no associated ascertainable disease of the hepatic parenchyma This suggests that in disseminated lupus erythematosus marked increase in the permeability of the sinusoids leads to increased output of lymph The present patients with a clinical syndrome strongly suggestive of disseminated lupus erythematosus experienced a massive insult to the hepatic parenchyma that histologically resembled acute and subacute viral hepatitis in 3 instances and resulted in postnecrotic cirrhosis in 2 instances In view of these facts other explanations of these bizarre cases deserve consideration

Until a specific test for the virus of hepatitis is perfected the possibility that the present patients had two diseases, namely disseminated lupus erythematosus and superimposed viral hepatitis, cannot be completely ruled out Furthermore despite what appears to be overwhelming clinical and laboratory evidence of disseminated lupus erythematosus the possibility that the syndrome is representative of an unusual

form f primary d sease of the liver must be considered.

Serum Glutamic Oxalacetic Transaminase in Dermatomyositis. A ses ment of the degree of clinical activity of dermatomyositis is difficult, because the cutaneou fin l ngs and myo itis pursue thei own courses with no apparent relation between the degree of acti ity in either Ordinary laboratory fi dings are not correlated with the acti ity of the process, and e en urinary creat ne and creatinine excretion studies are not as reliable guide of clinical acti ity a wa formerly presumed.

Ele ation of serum transaminase lev ls appears to be related to inj ry or destruction of certain tissues with release f the enzyme into the serum. Serum transaminase activity has been found to be levated in patients w th muscle d sease particularly dermat myos tis. José M de Moragas, Harold O Perry and Gerard A. Fleisher[2] (Mayo Clin c and Found.) tudied serum transaminase activity i 17 patients with dermat myositis. Three patients with disease in the inactive phase had normal level 14 with active disease had high levels that were, in some cases extreme The average for 50 normal subjects wa 1.01 μM /hour/ml Some patients with ct dermatomyositis had levels 10 times as high. In 4 pat ents clin cal improvement was accompanied by decreasing values of the serum transaminase

Serum transam ase determ nations appear to be a useful index of linical activity n dermatomyos tis and are an aid i diagnosi However the authors stress the nonspecificity of serum transam nase ctivity in dermatomyositis The acti ity may be elevated in conditions, such as systemic lupus erythem t sus, which are considered in the differential diagnosi f dermatomyos tis. Normal serum transam nase levels ould make a diagnosis of act ve dermatomyositis unlikely

[While this test is obviously not specific for dermatomyositis, it is nevertheless one more procedure which can be utilized in the differential diagnosis of this disease —Eds]

Diffuse Scleroderma Clinical Study of 65 Cases is presented by Zdenek Stá a (Charles Un v Prague) Acrosclerosis was present n 57 women and only 3 men, whereas diffuse generalized scleroderma occurred in 2 women and 3 men. Apparently diffuse scleroderma of the acrosclerotic

(2) J.A.M.A. 165 1936-1938, Dec. 1 1957
(3) Dermatologica 117 135-47 September 1958.

type is almost exclusively a disease of women. In most patients Raynaud's phenomenon occurred first between ages 20 and 30 whereas onset of sclerodermatous changes was most common between ages 30 and 40 In 30% of cases acrosclerosis occurred in women with premature menopause or marked menstrual disturbances. Almost one third of married women with acrosclerosis were childless and another third had only 1 child

The common clinical findings in patients with acrosclerosis included Raynaud's phenomenon heightened perspiration mainly of the palms and feet, hardening of the skin sclerodactylia masklike facies trophic ulceration of the finger tips and over joints paronychias and trophic nail changes trophic hyperkeratoses over joints and bony prominences mutilations of the fingers hyperpigmentation telangiectasia of the face neck and even the extremities joint manifestations muscle pains and pain in the feet when walking Less common findings were sclerostomia, microglossia paradentosis atrophy of the gums and alveoli decay and loss of teeth radial perioral wrinkles dysphagia headache and keratoconjunctivitis sicca.

Internal x ray endocrinologic, neurologic and laboratory examinations indicated that advanced acrosclerosis can actually be considered progressive systemic sclerosis. In vivo this sclerosis can be proved only with difficulty in most internal organs although sclerosis of the lungs and esophagus can be demonstrated in many patients. So-called sclerodermatous heart disease is difficult to diagnose on the basis of the ECG In the present group in contrast to previous reports serum calcium and phosphorus levels were within normal limits. Blood counts were normal but sedimentation rate and dysproteinemia increased in proportion to progression of the acrosclerosis

Prognostically it is important in acrosclerosis that the extent and degree of involvement of internal organs do not always parallel the severity of the sclerodermatous process.

Raynaud's Syndrome Acrosclerosis Scleroderma In the course of long standing Raynaud's disease sclerodermatous changes of the hands may develop which are identical with the initial stage of diffuse scleroderma. According to S Ja

blonska, B Bubnow and B Lukasiak[3] (Warsaw Med. School) when d fferentiation between scleroderma-l ke changes in Raynaud s disease and early scleroderma is dif ficult or mpossible on clinical grounds, a decisive clue may be fforded by function tests, particularly by determination of sensory chronaxy of the skin.

In normal cond tions, sensory chronaxy values vary be tw een 0 1 and 0.6-0.8 sigma, depending on the site. In various kin diseases chronaxy is prolonged in the skin lesions de pending on the morphologic character of the changes Only in scleroderma, circumscribed as well as diffuse, is it prolonged n seem ngly healthy skin and in the lesions much more so tha in ther diseases. In diffuse scleroderma chronaxy is prolonged in the lesions to 2.5-10 sigma and varies in the seemingly healthy skin between 1.5 and 7 sigma. In circum scribed scleroderma, the indexes are usually lower (within the foci 1 5-7 igma and in the healthy skin 1 5 sigma) In long-stand ng Raynaud s disease with sclerodermatous hanges n the hands, clinically indistinguishable from scle- rodactylia, hronaxy is prolonged in the affected skin but this is of no significance since it depends only on the mor phologic character of the lesion. It is absolutely normal in the rest of the skin.

Capillaroscopy is also of some accessory alue, for it re- eals two entirely different pictures in Raynaud s disease and in diffuse scleroderma In Raynaud s d sease the capillary loops are extremely dilated and enlarged with irregular in dented outlines and aneurysmal dilatations of the walls The blood stream l slow and vascular reactions to physical stim ul e reduced. I scleroderma the number of loops s sub- stantially decreased, the capillaries are markedly deformed and occasionally only parts of loops are vis ble. The blood tream is slow and beaded, with frequently visible large gaps. Reactions to physical stimul are usually suppressed. In cases of pseudosclerodermatous change n Raynaud s disease of long duration angiospastic changes of th arterioles over many years and proliferation of collagen obliterate the lu mens f the capillaries by strangulation so some of the loops are deformed, shortened and thin, and the blood stream is slow and beaded. However these changes are never so pro-

(3) Brit. J. Dermat. 70:37-43, February 1958.

nounced as in true scleroderma with concomitant Raynaud phenomenon and most of the loops show none of the typical dilatation of the central part nor indentation and aneurysms of the capillary walls and the distinct increase in size which are typical of Raynaud s disease.

The authors conclude that so-called acrosclerosis is in fact, a typical diffuse scleroderma with prevalent changes in the upper extremities and face coinciding with Raynaud s phenomenon The term "acroscleroderma is much better than acrosclerosis since it indicates a connection with scleroderma. However it does not seem useful to restrict the term acroscleroderma to cases in which Raynaud s phenomenon precedes the development of scleroderma and in which the disease runs a slow course. The distinction between acroscleroderma with and without concomitant Raynaud s phenomenon can be accepted in principle, but there are no essential differences between the two varieties They run an identical course and Raynaud s phenomenon may appear at any stage or remain absent

► [The very distinct differences in th chronaxy values bet een diffuse and localized scleroderma, on the one hand, and long-standing Raynaud's disease with sclerodermatous changes, on the other and the differences in the capillaroscopic picture would seem to justify ontinued differentiation between these two conditions The fact that in some cases it i not possible clinically to differentiate clearly between them not a convincing argument against this point of iew The primary proces appears to be in the blood vessels in Raynaud disease with sclerodermatous changes and in the connective tissue scleroderma —Ed.]

Cancer of Lung in Progressive Systemic Sclerosis. R. L. Richards and J A Milne[6] (Univ of Glasgow) report 2 cases in which cancer of the lung was associated with progressive systemic sclerosis (generalized scleroderma) and review 4 similar cases from the literature Of the 6 patients 5 were women and were known to have had systemic sclerosis for many years before they died of carcinoma In at lea t 4 pulmonary manifestations had been present for a considerable time. Therefore, it is postulated that in these patient pulmonary fibrosis was a premalignant condition in which neoplastic changes eventually developed All 5 women showed diffuse interstitial changes of progressive systemic sclerosis in parts of the lungs unaffected by carcinoma but cystic changes were present in only 2. All 5 had adenocarcinoma

(6) Thorax 13 238-245 September 19 8

or al eolar cell carcinomas, types which are thought to be na sociated with cigaret smoking or other irritant factors.

One of the patient with ca cer of the lung and progressive system c scleros is had a clinical picture different from that f the other The patient was a man who had a rela ti ely short history Until the terminal stages th re wa no idence of pulmonary disease At autopsy the part of the lungs unaffected by t m r did not how either interstitial fibros or cystic changes of progress ve sy temic sclerosis In this case therefor the tumor and the cutaneous and as cular manifestations of progressive systemic sclerosis appear to ha de eloped together in a patient with previously normal lungs. F rth r thi is the only case m whicl the tu mor was a bronchial carcinoma f the mall cell t pe which bel eved to be a sociated with cigaret smoking

Study of th literature revealed no good evidence of an intimate association between malignant disease n general and progressi e systemic scleros such a is found in some cases of dermatomyos tis. In most recorded cases in which neopla m and sy temic scleros coex ted, the a sociation appeared to be fortuitous. Th makes it more likely that in the 5 patients in whom espiratory man festati ns of systemic sclerosis preceded onset of malignant disease by several ea there was som d rect connection between the pulmonary changes of progres e y tem c sclerosis and the de- lopment of lung can er

[It is of course, difficult to decide hether in these cases the malignant changes er an outgrowth of premalignant sclerosis in the lungs or hether there as fortuitous occurrence of sclerosis and cancer in the same patient, or hether there as an association between malignant disease and scleroderma, such as is found in dermatomyositis.

Lichen sclerosus et atrophicus is another sclerotic process in hich malignant changes occur in exceptional cases involving the ulva Her again one must ask can lichen sclerosus et atrophicus be premalignant condition or is the development of ulvar carcinoma in this condition fortuitous or perhaps precipitated by some third factor —Eds]

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9 DISEASES OF THE HAIR

Is Alopecia Areata Psychosomatic? Psychiatric Study of 125 unselected patient i presented by Ida M calpine[7] (St.

(7) Brit. J Dermat 7 17 34 ... 1958

Bartholomew's Hosp London) Included were 14 patients with alopecia totalis and 11 with alopecia universalis. Five patients were under age 10 52 were aged 10-29 and 68 were over 30 Fourteen had had other dermatologic conditions, 6 had had other illnesses (gross obesity diverticulitis, peptic ulcer pernicious anemia tuberculosis and thyrotoxicosis) • and 5 had had major operations In 3 patients, alopecia areata followed stitching of a scalp wound In 6, the condition followed childbirth and in 1 two attacks of alopecia occurred only during two pregnancies with subsequent recovery In 12 another member of the family had had alopecia areata.

No psychiatric abnormality was found in 84 patients (67%) 27 patients (22%) were considered to have a mild psychiatric disturbance qualifying for the label neurosis and 14 (11%) had a severe psychiatric disturbance in the past or at present qualifying for the label "psychosis." If psychologic factors play a significant etiologic role in alopecia areata, the highest incidence of mental disturbance would be expected in the severest forms of alopecia if only because they usually result from repeated attacks. However the largest percentage of patients with alopecia areata and totalis or universalis occurred in the psychiatrically normal group and the lowest percentage in the psychosis group A greater portion of patients with alopecia totalis or universalis were mildly disturbed than of those with alopecia areata. To establish whether this is significant in showing that psychologic factors are important the author further compared the duration and number of attacks of alopecia with the degree of mental disturbance. There was no significant correlation The somewhat higher incidence of mild mental disturbance in patients with the severer forms of alopecia may therefore be due to chance or to factors such as the increased liability to social embarrassment and isolation of severe alopecia. Thus it may be regarded as more effect than cause

Only 1 of the 14 patients with severe psychiatric disturbance gave a clearcut history of alopecia developing at the time of mental breakdown with subsequent remission of both Six of the total group gave histories of mental or emotional trauma to which their alopecia had been attributed However careful investigation showed that episodes of stress by no means coincided with or were followed by at

tacks of alopecia. Those which might have been pathogenic were not followed by attacks and when alopecia was established it was not significantly influenced by amelioration or development of mental stress. Where patients gave a history of mental stress preceding an attack of alopecia, close scrutiny of their lives before and after revealed many other situations of equal or greater stress which had not been followed by alopecia.

Psychotherapy was used in treating 35 patients who showed some degree of psychiatric disturbance. Though many improved, both in their attitudes to themselves and in their social relations, in none was the alopecia influenced in any way. Psychotherapy did prove helpful, however, in overcoming anxiety and depression caused by the baldness.

The author concludes that the investigation produced no evidence for the widely held view that psychologic factors play a significant part in causing or precipitating alopecia areata. The occurrence of alopecia areata in mental defectives also contradicts any significant etiologic role of psychologic factors or mental trauma.

► [Macalpine's study strongly speaks against the suggestion or assumption frequently made in the dermatologic literature and textbooks that psychogenic factors are important in the etiology of alopecia areata and its more extensive variants. As is probably well known by now, the present editors of this YEAR BOOK and their immediate predecessor for many years has taken a critical attitude regarding the *indiscriminate* use of psychosomatic factors to account for various dermatoses of unknown or partially known causation.—Eds.]

Sudden Graying and Psychic Trauma in Alopecia Areata is discussed by G. Klingmüller[8] (Univ. of Bonn). It has been assumed that in aging the previously pigmented hair does not become secondarily apigmented but that it is replaced by gray hair. Sudden graying of the hair was observed in the following patient.

Man, 62, felt slightly dizzy and excited, as he had many times before. Four days later he noticed on the right neck some loss of hair in a round area. Within the next 3 days he lost, over night on his pillow and in the morning while combing, bunches of black hair. Simultaneously he lost his dark eyebrows and beard hair. Before his sudden hair loss, his dark scalp hair was mixed with gray hair. After 3 days, when he had lost all his dark hair, he started losing, though much slower, his gray hair.

On hospitalization, the general and neurologic examinations were negative. The scalp hair was very thin, sparse, the hair evenly white.

(8) Dermatologica 1 7-44, 2, August, 1958

The scalp was hypotonic, felt fatty and when studied with a magnifying glass showed in many follicles black, 1 2 cm. long hair stumps, which could be easily expressed. The fingernails were normal. Subsequently the patient lost all his body hair Alopecia areata manifested itself during the follow-up period Rich white hair appeared, mainly in the occipital region in circular areas

Thus in the patient studied an acute alopecia areata caused the pigmented hair to fall out rapidly whereas the white hair remained longer giving the appearance of the hair becoming white rapidly No psychic trauma preceded the graying

► [A very reasonable explanation of the phenomenon of sudden graying of the hair Ephraim at the Skin and Cancer Unit observed a somewhat different sequence of events his patient first developed sudden graying of the hair and soon thereafter was found to have vitiligo! The occurrences described by Klingmuller and Ephraim may well furnish explanations for some of the other cases of sudden graying which have been reported from time to time —Eds]

Alopecia Perinaevica For 9 years M Quiroga and V Pecoraro[9] (Buenos Aires) observed 2 men and 1 woman aged 28-48, who had alopecia areata with a central pigment nevus (Fig 20) Each patient presented only 1 focus of alopecia, suggesting that the inhibiting factor causing the hair loss has to be sought in the nevus. The changes in the hair itself



Fig 20.—Papillomatous pigment nevus in center of alopecia areata spot in man, 48. (Courtesy of Quiroga, M and Pecoraro, V Hautarzt 9 377 378, August, 195)

(9) Hautarzt 9 377-378 August, 1958

ndicated the same mechanism of hair loss as n the usual f rms of alopecia areata.

These findings could be compared with those in vit ligo

v tiligo proper

The alopecia permaer ca may furnish further proof for the mption that alopecia areata and vitiligo are both the results f a s m'lar mhibit ng neurotrophic acti ity Thi ac t ty may occasionally emanate from a ne us itself

► [Another piece of evidence suggesting a close relation between alopecia areata and vitiligo However there are other possible mechanisms besides "neurotrophic activity which could underlie both diseases —Eds]

Traction Alopecia. The dermatologi t ha long been aware that per istent and prolonged traction of the ha r may produ baldness. Many recent writ ngs de oted to care f the scalp and hair warn of the necessity of avoidi g prolonged traction but desp t these dmonition the pony-tail hair ty1 has remained popular

In th past 3 year Albert H Slepyan[1] (Uni of Ill nois) bserved 24 cases f alopecia of the scalp in young girl wearing the pony tail. The earliest mar festation is a mild erythema about the f llicles receiving the greatest amount f traction Occa ionally som scaling is noted In some cases minute folliculopustules occur in the erythematous rea After several months, along th margin of the hairlin the part of the hair occasional hairs appear m ssing gi ng the rea a plu ked look (Fig 1) In well-estab-l hed cases small o al or l near areas of baldness radiate in th direction of traction. By the time alopecia is ev dent, the scalp no lo ger appears reddened or scaly at these s tes In som cases the scalp has ppear thin ed, w thout evidence of gross baldness. Since som patients wea bangs, with the part l 3 i behi d the frontal hair ma gi inflammation or lopecia may occu at these sites. Other areas of predilection re the m dl of the scalp preauricula postauricular and nuchal ones.

I all but of the 4 case the alopecia disappea ed w thin months after the ha r tyle was changed and traction was l ed. In these 2, the alopecia seemed less extensive

(1) A.M.A. Arch Dermat 78 395 396, September 1958



Fig 21 —Marginal lovel ement giving postauricula and mental rea "pinched look. (Courtesy of Slepyan A. H A M A Arch Dermat 7 395 39?, September 1958.)

than when first seen but the remaining alopecia appeared complete

The term traction alopecia is suggested to describe those conditions which were hitherto designated as alopecia limi nari frontalis, traumatic marginal alopecia and others in which persistent traction with its resultant inflammation and the sequelae of inflammation can be established.

Unique Case of Trichorrhexis Nodosa ("Bamboo Hairs") is presented by Earl W. Netherton[2] (Cleveland Clinic)

Girl, 4 had dry ichthyotic skin and generalized scaly dermatitis. The eruption had been present since birth and was compatible with a diagnosis of erythroderma ichthyosiforme congenitum. The hair on the scalp was dry fragile and lusterless. Hairs on the occiput and sides of the scalp were no longer than 3-4 cm. and fractured so easily that it was difficult to remove them from the follicle by traction.

Microscopic examination of hairs from the scalp and eyebrows revealed nodose swellings varying greatly in size. The earliest indication of abnormality was a narrow indentation of the cortex of the hair forming shallow sulcus, which appeared to surround the shaft. As the abnormality progressed, swellings of the shaft developed, the sulcus enlarged, and on the proximal portion of the hair shaft, concavity formed into which fitted the adjacent enlargement of the distal portion of the hair These combined changes resulted in formation of pseudo-jointed nodose swellings resembling the joints of a bamboo pole Cultures of hairs showed no growth of fungi.

Examination of the patient 7 years later revealed the same nodose swellings of the hair shafts. The scalp hair was still dry lusterless, and abnormally short.

This patient's fragilitas crinium and concomitant eruption are considered to be essential components of a congenital ectodermal defect. As in monilethrix, the primary hair disturbance probably occurs within the hair papillae A biopsy specimen of the scalp was not obtained. Several eminent dermatologists stated that they had not seen similar nodose swellings of the hair shaft.

Nylon Brush. Agnes Savill reports several cases of hair loss resulting from use of hair brushes with nylon bristles. In most cases an area of alopecia appeared over the vertex. Examination revealed short hairs with frayed ends in the bald area. In each case alopecia cleared rapidly when nylon brushes were discarded and bristle brushes substituted.

In recent years the old fashioned hair brush has become rare because the bristles taken from hogs and wild boars of

A M A Arch Dermat 78 443-447 October
Rev J Dermat 78 296-299 Aug Sept 1958

Siberia and the coldest regions of Manchuria are now difficult to obtain. Nylon brushes have bristles composed of nylon monofilaments cut to the required length. This process can leave an uneven square end which is injurious to the hair. Some manufacturers have succeeded in producing a rounded end which is safe to use. Other firms have replaced nylon with molded polyethylene quills which are smooth, resilient and have rounded ends. This insures that the hair shafts do not become entangled, frayed or pulled out by the roots.

► [In recent years we have seen an increasing number of young and middle-aged women with diffuse alopecia of the scalp (see comment to article by Skog, p. 436). However, nylon brushes did not seem to be the causal factor in our cases.—Eds.]

Keratodermatitis Follicularis Decalvans. According to *Frederick Reiss, Milton Reisch (New York)* and *Constance Millett Buncke*[4] *(San Mateo, Calif.)*, mention is made of follicular hyperkeratoses associated with cicatricial alopecia in the European literature, but few cases have been reported. In the American literature, except for Graham Little's disease *(lichen planopilaris)*, consisting of the triad of lichen planus, acuminate follicular lesions and alopecia, no mention is made of a condition corresponding to that described in the following report.

Woman, 69, had pruritus and partial loss of scalp hair of 3 months' duration. Past history was negative except for diabetes. Examination revealed partial but diffuse alopecia of the scalp and the outer third of the eyebrows. Hyperkeratotic follicles were present in the area of [illegible] could be pulled out with ease [illegible] gement were [illegible] There were [illegible] tic, slightly [illegible] of the arms [illegible] of observa[illegible] mucosa was normal.

The patient received vitamin A orally and 5% ammoniated mercury ointment locally. A severe folliculitis developed. This subsided, but the hair continued to fall. Alopecia of the scalp and eyebrows was complete 15 months after onset of the eruption.

Microscopic examination of a lesion from the shoulder showed thinning of the epidermis in some areas. There was a patulous pilosebaceous orifice filled with keratotic plugs. In the corium, just below this, was an area of perivascular infiltration of lymphocytes, histiocytes and chromatophores. The sebaceous glands appeared normal.

(4) A.M.A. Arch. Dermat. 78:619-624, November, 195[illegible]

Almost all the follicular ostia in a specimen from the scalp were filled with lamellated horny material. Some of the follicula opening showed cup-shaped dilatation. Several follicles were devoid of hair. The outer root sheath was edematous. Perifollicular infiltrate was sparse and composed mainly of lymphocytes and occasionally histiocytes. There was distinct evidence of scar tissue more pronounced around the hairless follicles.

The authors feel that folliculitis decalvans alopecia cicatrisata, lichen planopilaris lichen spinulosus, lichen planus follicularis circumscriptus, alopecia mucinosa and keratodermatitis follicularis contagiosa can be ruled out on clinical histologic grounds. Certain finding resemble those seen in lichen (keratosis) pilaris. In extreme cases of the inflammatory type slight scarring may result but is rare. However lichen pilaris has its onset in early infancy and comes to standstill at maturity. Furthermore complete baldness has never been observed in lichen pilaris.

Ulerythema ophryogenes has certain features in common with the present case, particularly the cicatricial atrophy affecting the eyebrows and at times involving small areas of the cheek and scalp. The present case also has some features in common with cases observed by Lang and by Strassberg and designated keratodermatitis follicularis atrophicans. In these cases however the disease progressed rather slowly and did not produce complete baldness.

Noncicatrizing Alopecias With Special Reference to Alopecia Areata. William N. New and Walter R. Nickel[3] (US Naval Hosp San Diego Calif) point out that about 95% of all baldness is ordinary or common male baldness. There are three main interrelated etiologic factors in this type of baldness: heredity, gonadal influence and age. In sections of tissue from scalps with male baldness of long standing, the sebaceous glands were numerous and large and the sweat glands appeared normal. The number of hair follicles were reduced and the ones remaining were atrophic.

Diffuse hair loss may result from medicaments (thallium and other heavy metal salts, quinine, Atabrine[*], Cyrenin, barbiturates, arsenic, aminopterin, reserpine, coumarin, heparin, sulfonamides, thyroid antagonists such as propylthiouracil and massive doses of vitamin A) or disease states (hypothyroidism, iron-deficiency anemia in women, leukemia

(3) California Med 89 [illegible], November 58

diabetes debilitation impacted wisdom teeth focal and general infections acute systemic lupus erythematosus and fevers over 103 F) Women may have diffuse hair loss post partum or after the menopause

Alopecia areata is of special importance because 50% of the patients whose disease began before puberty eventually had alopecia totalis and 23% of those with postpuberal onset progressed to total baldness About 75% of both groups remain totally bald The cause and mechanism of production of alopecia areata is obscure, but the frequent association of psychic trauma is stressed by most authors Treatment is of little avail General use of corticosteroids is not recommended despite the improvement in scalp appearance observed in most patients in whom systemic administration of these hormones was used Alopecia areata occasionally is simulated by other types of baldness especially trichotillomania and alopecia resulting from use of hair waving solutions and hair straighteners

In 22 patients with alopecia areata studied microscopically by the authors the presence of huge, patulous orifices, devoid of hair and plugged with keratin detritus was a striking feature Plugging was more pronounced than in lupus erythematosus. The epidermis was normal except for absence of pigment. In the dermis a constant inflammatory change occurred composed of lymphocytes related to the hair follicles and blood vessels and in some instances to sebaceous and sweat glands In all instances there was a relative or absolute absence of robust hairs in the areas of alopecia. Inconstant changes included fibrosis at varying levels in the cutis in relation to the follicles, and an apparent superficial position of the sebaceous glands in instances in which there was no identifiable active formation of hair

► [Macalpine (this YEAR BOOK, p 261) was unable to substantiate the age-old claim that there is a connection between emotional factors and alopecia areata —Eds.]

Urticaria Pigmentosa Solitary Lesion. Aaron Kamm sky Jorge Dartsch and Jorge Abulafia[4] (Buenos Aires) report solitary mastocytoma in 3 children (ages 1 year 2 years and 6 months) the first such cases in the Argentine litera ture On case is described.

Boy 1 since birth had had on the upper thigh a single oval plaque 2×4 cm of reddish chamois color elevated, not hairy w th a slightly granulated surface Urtication occurred spontaneously and with scratching (Darier's sign) and spontaneous blisters appeared on several occasions. The pruritus was worse at night and disturbed the child rest. History general and hematologic examination and rays of the skull and extremities were normal.

Histologically this type of urticaria shows an intense in filtrat f ariable distribution n the dermus, consisting of mastocytes (demonstrated by metachromatic staining) In some cases these cells surround blood vessels and adnexa in loose clumps in others, in a subepidermal layer and in m the mastocytic infiltration is extremely pronounced.

Clinically the condition is characterized as follows. It appears n the first months f life or is present at birth. It has a nod le r pl que 2 3 cm. in diameter which varies from red dish brown to y llow Urtication occurs spontaneously or w th t auma, ften forming blisters o vesicles (an impo tant diagnostic sign) B th sexes are equally affected. The h tologic picture typical It beha es cl nically like a ne u which it esembles In time the lesion flattens, stops tching and f rms blisters and in the course of years may disappear altogether No case has been described in which additional lesions ha e appeared or the process became generalized

Apparently there i little knowledge of this interesting form of urticaria pigmentosa, especially among pediatricians Despit the pa city of reports it is probable that many cases emai undiagnosed and are confused with pigmented nei So fa no blood dyscrasias nor mastocytic foci in bones have been demonstrated in these cases of solitary mastocytoma. No effective treatment has been found. Antihistamines by mouth a d parenterally and corticosteroids in ointments

[4] Arch argent dermat 7 237 September 1957

and local injections relieve the pruritus but have no effect on the lesion

► [Solitary lesions of urticaria pigmentosa (mastocytoma or solitary mast cell nevus) have been described in increasing numbers (Chargin and Sachs A.M.A. Arch. Dermat. & Syph. 69:345 1954 and Drennan and Beare J. Path. & Bact. 68:345 1954) It would seem that lesions which have a tendency to recurrent vesiculation might be subjected to various investigations including histochemical studies in the attempt to learn something of the mechanisms which lead to blistering.—Ed]

Histamine and Related Compounds in Urticaria Pigmentosa Analyses of Tissues Having Mast Cell Infiltration. Lytt I Gardner and Artelissa A Tice[7] (State Univ of New York Syracuse) analyzed chemically tissue from the liver and spleen of a child with urticaria pigmentosa. Both tissues were infiltrated with mast cells Trichloroacetic acid extracts of tissue from the liver were chromatographed on paper Histamine was found in the tissue in several hundred times normal concentration and exceeded the values for human tissue reported in the available literature. Since the liver and spleen were extensively infiltrated with mast cells, it seems likely that the excessive histamine was localized in these cells

No serotonin could be detected in these human mast cells in contrast with previous reports of increased serotonin content in rodent mast cells and in agreement with the findings of Sjoerdsma and associates who could find no serotonin in skin from a patient with urticaria pigmentosa. The findings suggest that decarboxylation of 5-hydroxytryptophan to serotonin does not occur in the human mast cell Accumulation of compounds such as 5-hydroxytryptophan, kynurenine or hydroxylated kynurenine may take place instead Measurement of activity of xanthine oxidase revealed no gross increase in activity in the mast cell liver Activities obtained were so low that nothing further could be concluded

Acetone extracts of tissue from the liver were made and the residues chromatographed Besides histamine three substances of unknown structure resembling tryptophan and/or its metabolites were noted Concentration of heparin like material in the liver was greatly elevated and the observed histamine presumably was the organic base in association with the organic acid heparin Whether histamine or heparin plays the primary pathogenetic role in urticaria

(7) Pediatrics 21 805 812, May 1958

pigme tosa is unknown. Were either being o erproduced or u de co sumed, due to metabolic error increa ed co centra tions of the other compound in the tissues to sati fy the requ rements of the law of electroneutrality must be pre d ted S nce either histamine or heparin exert uch potent physiologic effects n extremely mall concentration in plasma, there would be some survival value in maintaining eat e amount of such compounds in n ntracellular pos tion

► [All presently available evidence indicates that the cutaneous mast cells in man contain histamine, heparin and hyaluronidase, but no serotonin. The question remains to be answered whether one or more of these substances or other as yet unrevealed substances in the mast cells produce the clinical manifestations of urticaria pigmentosa. Baer Bersani and Pelzig recently observed 3 patients with urticaria pigmentosa in whom the oral administration of reserpine produced peculiar clinical manifestations These included form of "flushing in 1 patient and lessening of wheals in 2 others The possibility that these effects are the result of degranulation of the mast cell granules by reserpine has been considered.—Eds]

Spontaneous Histamine Shocks in Urticaria Pigmentosa. (Bloom H Dunér B Pernow J Winberg and R. Zetterstrom (Karolinska Inst., Stockholm) report a case.

Girl, at birth, had four red macules about 1 cm. in diameter on the trunk. The skin lesions increased in number and size, and the color changed from blue red to brown. Clinically and histologically the lesions ere typical of urticaria pigmentosa. At age 3 months she had a sudden generalized blush, accompanied by extreme irritation, then shortly became pale, flaccid and unconscious. At about the same time heals appeared over the cutaneous lesions. Some of the wheals were transformed into blisters Unconsciousness lasted several minutes. This sequence of events occurred later on several occasions, but unconsciousness occurred only tw ce. At age 10 months, tw tumors about half the size of hen' egg ppeared on the skin (Fig 22) At this time pruritus was almost unbearable One tumor was removed surgicall without clinical improvement. Hydrocortisone 1.5 mg daily as injected into the second tumor for 9 days. N macroscopic change occurred in the tumor and no clinical improvement followed, so the lesion was excised urgically A few days later tching and attacks of restlessness disappeared Microscopic examination of the tumor revealed definit regressive changes in the mast cells resulting rom local administration of hydrocortisone.

Examination 6 month later revealed no recurrence of the cutaneous tumor The histamine content of tw small skin lesions and urinary ex etion of histamine were markedly elevated. Urinary output of the 5-h droxytryptamine metabolite 5-hydroxyindole acetic acid was normal

Urinary output of free hi tam th patient (and n 7

Acta paediat. 47 133 142, March, 1958

and local injections relieve the pruritus but have no effect on the lesion

► [Solitary lesion of urticaria pigmentosa (mastocytoma or solitary mast cell nevus) have been described in increasing numbers (Chargin and Sachs A M A Arch Dermat & Syph 69 345, 1954 and Drennan and Beare J Path & Bact 68 345 1954) It would seem that lesions which have a tendency to recurrent vesiculation might be subjected to various investigations including histochemical studies in the attempt to learn something of the mechanism which lead to blistering.—Eds.]

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(7) Pediatrics 21 805-812, May 1958

liberation. This fact might be explained by the finding that histamine in vitro blocks the anticoagulant effect of heparin in proportions larger than 20 1

► [Flushing and burning can also be produced by 5-hydroxytryptamine. However the fact that no 5-hydroxytryptamine has ever been found in the mast cells of man, the absence of 5-hydroxyindole acetic acid in the patient urine and the increased urinary excretion of histamine speak in favor of spontaneous histamine shock in this patient.—Eds]

Association of Functioning Carcinoid Syndrome and Scleroderma I. Case Report is presented by Chris J D Zarafonetis, Stanley H. Lorber and Stephen M Hanson* (Temple Univ)

Woman, 42, exhibited paroxysmal flushing of the skin associated with telangiectasia and purplish red, raised, thickened areas on the cheeks and nose (Fig 23) scleroderma-like changes of the lower ex



Fig 23.—Purplish red, raised and palpably thickened areas on cheeks and nose. (Courtesy of Zarafonetis, C. J. D et al Am J M Sc. 236 1-14, July 1958.)

(*) Am. J. M Sc. 236 1-14, July 1958

others with urticaria pigmentosa) was abnormally high, which shows that in this disease there is not only local histamine release on mechanical irritation but also constant flow of this substance into the circulating blood. Thus on theoretical grounds the possibility exists that histamine



Fig. 22.—Not big, elevated, ulcerated lesion below left clavicle. This is one of tumor-like lesions which later was removed surgically. (Courtesy of Bloom, G. et al: Acta paediat. 47 152-162, March, 1958.)

shock may appear if release of histamine into the blood is suddenly increased.

Because the mast cells contain heparin and histamine it is surprising that there was no impairment of hemostasis in the present patient with massive histamine release, whereas in other patients severe and even lethal hemorrhages have been reported, with only minor symptoms of histamine

chronic endocarditis, pulmonary and tricuspid valvular stenosis, diarrhea and vasomotor disturbance. She also had a pronounced cutaneous lesion indistinguishable from pellagrous dermatitis. The extensor surfaces of the hands and forearms showed marked reddish brown pigmentation, with hyperkeratosis and scaling. From the knees to the ankles, sharply demarcated above, the skin was red brown, glistening and tightly stretched over the underlying tissues, which pitted on pressure. The skin of the dorsum of the feet and toes was pigmented and scaly. There was no abnormality of buccal mucosa, however, and no glossitis.

Much of the dietary tryptophan in this disease is diverted from its normal metabolic pathway and is used as a precursor of serotonin, thus inducing a relative deficiency of niacin. Treatment with nicotinic acid in daily doses of 150 mg resulted in a decrease in the pigmentation and scaling of the skin, but diarrhea increased in severity. As surgical treatment of the primary growth was not considered feasible, chlorpromazine, an experimental serotonin antagonist, was given in therapeutic doses, but it did not alleviate symptoms. The condition of the patient gradually deteriorated and she died about 5 years after onset of symptoms.

C rdiac lesions skin and vasomotor changes asthma and diarrhea are now ecognized a cl nical features of the car cinoid ndrome, and the l vel of 5-hydroxyindoleacetic acid th uri is regularly increased this disease. This biohemical feature makes possible confirmation of a presumpt l cal diagnos s.

The speed f growth and spread of carcinoid tumors ary but t ha been hown that th primary tumor can produce a detectable increase urinary 5-hydroxyindoleacetic acid bef re m ta tases occu Therefore, an attempt at surgical resectio is the first step in treating early cases. Since the disease apparently progresses lowly even after metastases ha e occurred, it may be of value to resect ny large secondary depos ts along with the primary growth to reduce the circulating blood level of 5-hydroxytryptam ne Numerous perimental serotonin antimetabol tes ha e been tried without gnifica t l cal o biochem cal improvement.

Cutaneous Manifestations of Carcinoid Syndrome are described b M in S. Zelickson[3] (Univ of Minnesota) Carcinoid t mor are most common in the small intestine though all part of the gastrointestinal tract below the esophagus, in l ding the gallbladder and appendix, may be involved. Reported extra-alimentary sites include the ovaries and

[3] Minnesota Med. 40 77 772, November 1957

tremities colicky abdominal pain and diarrhea, and cardiac murmur Attacks of flushing and edema could be precipitated by ingestion of small amounts of alcohol or by emotional stress. Autopsy revealed malignant carcinoid of the ileum with metastases to the liver lungs heart breast and appendix. Fibrotic changes were observed in the liver inferior vena cava, right heart, skin of the legs and in association with the tumor metastases.

The fibrotic changes observed in the liver inferior vena cava and right heart are those classically associated with functioning carcinoid tumors Sclerosis of the valves of the right heart is believed to be due to an excessive amount of serotonin produced in the hepatic metastases and released into the venous circulation Failure to induce similar alterations in the left heart appears to be due to destruction of serotonin by monoamine oxidase present in the lungs during the pulmonary phase of blood circulation

In view of the well-documented propensity of metastasized functioning carcinoid tumors to produce fibrotic changes in the right heart, it is surprising that little attention has been given to the possibility that similar changes may be induced elsewhere in the body In the present case, fibrotic changes were found in the skin and metastatic tumor sites. The presence of extensive scleroderma like changes in association with the other manifestations of fibrosis suggests the possibility that all these findings might be directly due to the functioning carcinoid tumor The association of these findings has been interpreted by Zarafonetis as a possible clue to the pathogenesis not only of the fibrotic changes of the functioning carcinoid syndrome but also of scleroderma and other fibrotic states It is theorized that such fibrotic changes result from a deranged interaction of the serotonin monoamine oxidase mechanisms at the tissue level

► [The search for the cause of scleroderma and related diseases requires imagination and ingenuity Although the association of scleroderma and functioning carcinoid syndrome in this case may well be entirely fortuitous it provides a lead which deserves further investigation MacDonald, Robbins and Mallory (Proc Soc Exper Biol & Med 97 334 1958) reported that dermal fibrosis can be deliberately produced by subcutaneous injections of serotonin creatinine sulfate in rats —Eds]

Carcinoid Syndrome with Pellagrous Dermatitis. J M Bridges J B Gibson Lavinia W Loughridge and D A D Montgomery[1] (Belfast) report a case

Woman, 60 had a malignant carcinoid with hepatic metastases.

(1) Brit. J Surg. 45 117 122, September 195

with interspersed blue areas. In this stage the picture is one of macular patchy purple cyanosis alternating with some areas of great pallor and others of brick red color nearly always confined to the face, neck and extremities. The flush may last 7-8 minutes and is usually accompanied by severe palpitation, tachycardia, bronchospasm and diarrhea. Later in the disease course the cutaneous changes become irreversible constant and generalized. The patient looks polycythemic and extremely plethoric because of permanent hyperemia of the face and neck with distended veins and profuse telangiectasia.

A pellagrinous type of dermatosis has been noted in some patients with malignant argentaffinoma. The lesions may look more pruriginous and less pigmented than those of true pellagra, but diarrhea, glossitis, mental torpor and the typical pigmentation and scaling of exposed parts may be found. It has been suggested that in the carcinoid syndrome all the available tryptophan is converted into 5-hydroxytryptamine and none is left for conversion into nicotinic acid. Lack of the precursor of nicotinic acid thus leads to development of pellagra.

Carcinoid metastases in the skin and subcutaneous tissues are rare. Three cases were found in the literature and the author has seen another. Palmar and plantar erythema in a patient with metastasizing argentaffinoma has been recorded and may be due to liver dysfunction. The same patient also had neurodermatitis and vitiligo. Another patient had acropachyderma.

► [The average dermatologist is unlikely to be confronted with the full-blown picture of metastasizing argentaffinoma because of the rareness of this syndrome. Nevertheless, it is of particular interest from the dermatologic viewpoint because of the pronounced cutaneous manifestations of flushing, erythematous macular eruption of the extremities and pellagroid changes of the light-exposed areas. Whereas much knowledge has been gathered about 5-hydroxytryptamine (serotonin, enteramine) and its occurrence in various species of animals and man, much remains to be learned about the actual physiologic, pathologic and clinical significance of this material in man.—Eds.]

Cutaneous Porphyria with Porphobilinogenuria: Review and Report of Case Treated by Chelation are presented by Sherwyn M. Woods, Henry A. Peters and Sture A. M. Johnson (U. of Wisconsin). The patient represented an ex

A.M.A. Arch. Dermat. 77: 39-147, Mar. 1958.

lungs The tumors are composed of argentaffin cells which are normally found in these various organs. The argentaffin cells secrete serotonin and glucagon Serotonin appear to play a definite role in the development of the syndrome Only about 20% of carcinoid tumors are malignant and the syndrome apparently occurs only in patients with metastases especially to the liver

Abdominal symptoms are usually the first manifestation of the carcinoid syndrome Cutaneous symptoms soon become prominent. Cardiac signs may not appear for many years The chief dermatologic manifestations are (1) reddish blue cyanosis of the face resulting from pulmonary stenosis, (2) telangiectasia over the central portion of the face (3) thickening of the skin and urticaria of the face and (4) bright to deep purple flush brought on by alcohol emotion, food spices or occurring with no apparent cause. The flush begins abruptly with rapid spread from the neck to the chest and face, including the conjunctivas and then to the upper arms There is increased warmth and a burning sensation in the parts affected with simultaneous bitemporal headache Symptoms subside after a period of 1 15 minutes leaving no residuals

Metastasizing Argentaffinoma from Dermatologist s Point of View According to Jean Walker[3] (Univ of Cape Town) cutaneous manife tations that have been seen in association with malignant argentaffinoma consist of vasomotor phenomena pellagrinou dermatoses palmar and plantar erythema neurodermatiti vitiligo and acropachyderma

The earliest and most obvious manifestation of the syndrome is a peculiar flu hing which may be confused with the menopausal hot flu hes of mi ldle-aged women The vascular symptoms may be tran ient r persistent but evanescent attacks of flushing are more characteristic A typical flush may be spontaneous or precipitated by alcohol cheese seasoned foods heat emotion tanding or manipulation of the lower bowel by enemas It alwa s starts with a subjective hot feeling and redness of the fa e quickly f llowed by the appearance of brick red pot on the limbs After 2 3 minutes the face becomes paler and the red spots may di appear or if the flush lasts longer they may become larger

(3) South African M. J 31 1271 1274 Dec 1 1 3

aluation of this type of treatment in cases of porphyria.

Clinical and Experimental Studies on Porphyrin Metabolism. First Report. R. Schuppli (Univ. of Basel) determ ed urinary porphyrin xcretion routinely n many pa t ent w th various skin diseases. No sex or age d fference was found between patients with and without porphyrinuria. S milarly extent of the skin lesion was not related to porphy rin ria. Among various internal a'lments only disturbed li r function seemed to influence porphyrin excretion. Most pat nt who had abnormal liver function tests excreted large mou ts of porphyrin. Among skin diseases all pa ti ts w th porphyria cutanea tarda excreted much porphy rin a w ll s coproporphyrin and uroporphyrin.

An interesting find ng was that among patients w th contact ec ema, normal e cretory values for porphyrins predominated and recurred almost with pathognomonic regu larit. Thu th author suggests that when eczematous patient excrete ncreased amounts of porphyrin some com plication may be expected.

About half the patients with actin c dermatoses showed normal porphyrin excretion. When these patients were studied separately according to the type of dermatosis the eczem atous form were found to be accompan ed by essentially normal porphyrin excretion whereas actinic dermatoses w th urt caria were often combined with porphyrinuria. Presence of the light-band substance of Kimmig does not alway mply light sensitivity. Its excretion in various skin l eases did not parallel that of porphyrin.

Porphyria was produced in rabbits with large amounts of allyl-isopropyl-acetyl-carbam de (Sedormid) but their skin d d not show any change in react vity when exposed to various physicochemical irritants.

Porphyria Cutanea Tarda. Tiong Hoo Tio (Surabaya, Indonesia) d B. Leijnse[6] (Rotterdam) describe a family in which 12 members in 4 generations were affected. According to Walden trom lassification, all the patients had porphy ria cutanea tarda. Application of the classification of Schmid, Schw rtz and W tson however causes some difficulties. Neurologic a d/ neurotic symptoms were found in 7 pa

5) Dermatologica 1 4 383 39 Apr May, 1956
6) A M Arch Dermat 72 164 176, May 1956

ample of hepatic porphyria cutanea tarda with evidence of latent and manife t porphyria in the maternal blood line First symptoms con isting of a vesiculobullous eruption on the exposed areas of the body after exposure to sunlight occurred when he was aged 16 He had mild hepatic impairment during attacks and spontaneously alluded to the correlation between his occasional use of alcohol and the onset of dark urine and skin lesions A liver biopsy specimen was histologically unremarkable.

The patient was studied clinically biochemically and histologically for 2 years during which time the emergence of porphobilinogenuria was observed with manifestations suggesting that the syndrome might be merging into that seen in mixed porphyria in which abdominal or neurologic manifestations may coexi t or alternate with cutaneous symptoms. Significantly elevated excretion of porphobilinogen and its precursor δ-aminolevulinic acid, was noted during a cutaneous exacerbation and even higher excretion wa present during asymptomatic remission Urinary excretion of these compounds in this patient not only suggested hepatic mixed porphyria but made likely the pos ibility of a future acute abdominal or neurologic episode and called attention to the absolute and mandatory avoidance of precipitating factors (alcohol sulfonamides barbiturates heavy metals etc) in management of such a case Failure to recognize this might re ult in the patient s death

Therapy with heavy metal chelates such as dimercaprol (BAL) and edathamil calcium sodium for acute intermittent hepatic porphyria has given highly favorable and often dramatic result in 14 f 21 cases seen by the author When the patient was daily given 1 Gm edathamil calcium sodium orally he had no cutaneous exacerbati n and said he felt more relaxed and mentally alert than ever bef re During the next summer he had no cutaneou le i n de pite repeated exposure to sunlight incidental t hi w rk He had no cramping constipation neurologi r p ychiatric difficulty Urinary excretion of porphyrin and precursors did not seem to be altered however by edathamil alcium odium therapy It is too early to speculate on the long term effectivene of the chelation therapy but the patient s apparent favorable response is encouraging and uggest the need fer further

evaluation of this type of treatment in cases of porphyria

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(7) Dermatologica 1 6 295 299 Apr May 1958
(8) A.M.A. Arch. Dermat 77 166 175, May 1958

tients and slight lassitude in 5 Many patients had abdominal symptoms and operations were performed in 7 Constipation was prominent in 5 These facts and the ages at onset (16-30) make it tempting to classify this family as having mixed porphyria though an acute attack with positive porphobilinogen has never been observed As the abdominal operations revealed abnormal conditions as it is common to find persons with odd behavior among the general population and especially as one nonporphyric member of the family was mentally abnormal the authors feel that this classification is not fully justified. Other writers have pointed out that no sharp distinction can be made among the several types of porphyria, and classification is sometimes only arbitrary

The genealogic table of this family clearly shows a simple dominant inheritance. Slight liver impairment was present in some patients All members of the family denied consumption of alcohol or barbiturates. All affected members showed hypersensitivity to sunlight Photophobia was found in 2 No patient showed any particular ocular defect. In 2 the diagnosis of porphyria could be confirmed only by fecal examination Three members of the family clinically became burned-out cases after about their 40th year

Cutaneous Form of Hepatic Porphyria and Porphyrin Excretion in Urine were studied by G Leonhardi and M Baer[7] (Univ of Frankfort) In disturbed porphyrin metabolism porphyrins accumulate which are intermediary products of hemin synthesis Alterations in porphyrin metabolism can be recognized clinically and chemically There is increased production of porphyrins that lead to changes in various organs, causing symptoms in the skin gastrointestinal tract and in the nervous system There also are disturbances in porphyrin metabolism which do not cause clinical symptoms. In both instances, the porphyrins are excreted by the kidneys and may be detected in the urine It has been shown that in various forms of disturbed porphyrin metabolism there are certain differences in the urinary excretion of porphyrins.

The authors studied the urinary porphyrin and their isomers in 8 patients who had the cutaneous form of hepatic porphyria The porphobilinogens ether soluble porphyrins

(7) Arch. klin. u. exper Dermat. 207 554 575 1 58

and ether insoluble uroporphyrins were determined quantitatively and the *porphyrin components* and their isomers were differentiated by paper chromatography In every patient, urinary excretion of uroporphyrins was increased Some increase in urinary coproporphyrins and traces of proto- and deuteroporphyrin in the urine was observed. Two patients also excreted porphobilinogen, 1 of whom had symptoms of the combined form of hepatic porphyria in his clinical history

Uro- and coproporphyrin isomers were estimated by intensity of their fluorescence by paper chromatography and were predominantly of type I

In cutaneous forms of hepatic porphyria, *the liver* performs the decarboxylation and dehydration of uroporphyrin to protoporphyrin incompletely causing hemin synthesis in the liver to stop at the stage of uroporphyrins. The manifestations of the disease may be due to disturbances in the enzyme systems of the liver

Hypertrichosis, Melanosis and Circumscribed Dermatosclerosis Consequent to Subcutaneous Injection of Hematoporphyrin Followed by Solar Irradiation were seen by Xavier Vilanova and Joaquin Piñol (Univ of Barcelona) in 2 patients. These cases support the hypothesis that skin *changes in porphyria* are the result of a *local reaction to deposits* of porphyrin in the skin.

A year before admission, woman, aged 40, received subcutaneous injections of hematoporphyrin solution in both arms as treatment for a psychic depression. Two months after the last injection on the day following sun bath, circumscribed inflamed areas, accompanied by swelling and severe pruritus and corresponding to the site of the previous injections, were noted on both arms. Symptoms gradually subsided, leaving dark, depressed and indurated plaques.

Examination showed dark brown, hard, board-like plaques, slightly oval, about 12 cm in diameter with a papular surface, they were freely movable over the deeper planes. The plaques also displayed striking hypertrichosis with long, coarse black hairs limited strictly to the indurated pigmented surface. Biopsy showed, in the *papillary body and corium*, bands of collagen, compressed and lacking in fine structure, with sclerotic, cicatricial appearance. Between these bands numerous fibroblasts were dispersed without constituting foci of infiltration. The elastic network had disappeared and capillaries were scant. The hypodermis was strikingly fibrosclerotic. The interlobular septa were enlarged fibrosis penetrated the fat lobules, which were reduced to a few

(1) Dermatologica Rev mex. 1 144-154, Oct-Dec 1956.

vesicles of fat surrounded by connective tissue fibers in some places and edema in others with the presence of lipophages. In fibrotic areas, principally in the cutis fine dark red granules were scattered diffusely these were interpreted as the remains of injected porphyrin. Pigmentation of the plaque was explained by an abundance of pigmented cells in the basal layer from which pigment extended toward the mucous layer across arborescent prolongations of melanocytes. Dermal melanophages were absent. The epidermis was perhaps slightly thinned and had an almost linear border due to sclerosis of the papillary layer The basal layer showed small areas of softening

► [In view of the fact that localized areas of scleroderma are sometimes seen in porphyria, the report of sclerodermatous changes produced by the local injection of a porphyrin solution into the skin is of special interest —Eds.]

Tongue Pigmentation in Addison's Disease. K Kitamura and Y Mishima* (Univ of Tokyo) report a case

Woman 44 for about 2 years observed a slowly developing brown discoloration of the skin all over the body Increased excretion of mineral corticosteroids in the urine was noted. On physical examination, the skin showed black brown pigmentation over the entire body Characteristically there was increased pigmentation on the extensor surface of the end phalanges as well as brown discoloration of the creases of the palms and soles, which otherwise were not pigmented. The lips were violet gray with many black dots. The entire oral mucosa showed gray brown discoloration The whole tongue was covered with dark violet-gray macules. The bulbar conjunctiva bilaterally had rice kernel-sized pigmented spots and the lid margins had similar pigmented dots.

Biopsy of a skin specimen from the right leg revealed extensive melanin deposits in the basal layer of the epidermis down to the middle layers of the stratum spinosum Rare chromatophores were noted in the upper layers of the corium. The dopa reaction revealed quite a few melanocytes in the basal layer but the chromatophores in the corium were dopa negative H stologic exam nation of the tongue pigmentations showed no remarkable pigmentation in the epithelium, whereas the papillary bodies of the mucosa below it were saturated with partly intracellular brown-black pigmented granules. Dopa staining revealed dopa positive melanocytes only in the epithelial cells close to the papillae, whereas the pigmentation under the papillae in the stratum papillare was exclusively dopa negative

Dependence of the papillary pigmentation on the melanocyte accumulation above the papillae suggests that the melanocytes which are in a resting state in the basal layer of the suprapapillary epithelium are activated by corticosteroid produce melanin and discharge it as papillary pigmentation

► [While pigmentation of the buccal mucosa and gum not uncommon in Addison's disease pigmentation of the tongue appears to be rare The authors state that administration of cortisone for 1 month caused lighten

(9) Hautarzt 8 484-486, November 1957

ing of the skin color on the entire body but they do not report hat happened to the pigmentation on the tongue —Ed]

Black Hair Tongue Comparative Study of Black Hair Tongue, Geographic Tongue and Drug Eruption of Tongue, based on cl nical and histologic find ngs and a review of the l terature is presented by Louis H Winer[1] (Uni of Cali f rnia, Los Angeles) In black hair tongue (F g 24) the flora of the mouth, by increasing acidity inh bit the kera tin se from desquamating stratum corneum. The color i not



Black hair tongue (Courtesy of Winer L. H A M A Arch Dermat 77 97]43 January 1 58)

l e t melanin but to keratin and the oxidation products of the oral flora Black hai tongue may be any color from yel low t black. Yellow lesions contain less bacteria and more keratin, whereas dark brown to black lesions contain not onl ncreased keratin but also more candida organism

Geographi tongue, clin cally because of its frequent e-currence configuration, progress and histopathologic fea t es resembles a benign type of superficial pyoderma, not unl k that of erythema streptogenes or so-called pityriasi mplex Geographic tongue s an atrophy of th fil form papillae d most likely to exces alkalinization and in fection of the erlying epithel um. The epidermal rete of geographic tongue about the same thickness as that of bla k hair tongue f th tratum corneum is excluded.

Orally admini tered tibiotics may produce epithelial hy

[1] M A Arch Dermat 77 97 10 January 958

Clinical Manifestations and Microscopic Findings of Black Hair Tongue, Geographic Tongue and Drug Eruption

	Black Hair Tongue	Geographic Tongue	Drug Eruption
Clinical Manifestations			
Location	Central posterior dorsum	Anterior lateral margins	Nonspecific
Duration	Persistent	Evanescent	Acute
Symptoms	Pasty taste	Burning	Burning
Type of lesion			
Patches	Yellow, brown, black, surface smooth to rough	Atrophic, smooth red center; gray elevated borders	Smooth
Border	Irregular	Arciform	Sharp; annular
Microscopic Findings			
Involvement	Filiform papillae	Filiform papillae	Entire surface
Stratum corneum	Increased and elongated cornified epidermal cups	Denuded, elevated with many P.M.N.'s	Parakeratotic, very thin
Epidermal rete cells	Spindle-shaped, clear keratinizing cells; intensely vacuolated	Slightly vacuolated; round	No change in size; thickened
Basal zone	Intensive increase in number of nuclei; small, round, or cuboidal cells	Normal nuclei; columnar cells; epidermal cutis junction invaded by P.M.N.'s	Normal nuclei, columnar cells
Cutis	No changes	Inflammation in papillary bodies	Edema, lacunal proliferation; many eosinophils and P.M.N.'s
Treatment	Vitamin A; painting with 20% podophyllin in acetone, alcohol or trichloroacetic acid	Dilute HCl; antibiotic; mouth wash	Interdict causative drug; steroids

pertrophy of the filiform papillae Parenteral penicillin may produce proliferation of the capillary endothelium eosinophilic invasion in the perivascular areas of the papillary cutis and parakeratosis without hypertrophy of the stratum corneum The epidermal rete in drug eruption of the tongue is

twice the thickness of that seen in black hair tongue or geographic tongue. The cl nical and microscop c findings in black hair tongue geographic tongue and drug eruption are compared in the table.

In 4 patients with black hair tongue painting with 20% podophyllin resin in equal parts of acetone and alcohol resulted in clearing in 2 weeks. The patients were given vitamin A troches to prevent recurrence. It is believed that after desquamation is accomplished, vitamin A locally applied ma interfere with sulfhydryl metabol sm, thereby inhibit ng recurrence of the keratosis of black hair tongue Of 3 patients with geographic tongue 2 responded to 250 mg hlortetracycline dissolved in 120 cc. water used as a mouth wash twice daily The third patient gave a history of indigestion due to achlorhydria. By administration of 1 cc. dilute hydrochloric acid 3 times a day both the indigestion and geographic tongue disappeared. A patient with drug eruption f th tongue responded to steroid therapy in 1 week. He was given 300 mg cortisone the 1st day 200 mg the 2d day and 100 mg daily thereafter

► [The author' clinical description indicates that the term "black hair tongue, although generally accepted, is ery inadequate name for these lingual changes The lesions are often neither hairy nor black. The finding that local Aureomycin therapy is beneficial in some cases of geographic tongue is interesting There is no evidence that geographic tongue is due to infectious micro-organisms and ordinarily the involvement is of many years duration —Eds]

"Linea Fusca (Brown Forehead Ring of Andersen, Wernoe and Haxthausen) Thirteen Cases are reported by P J Michel[3] (Lyons, France)

The fi t cases f this peculiar brown arch on the forehead, reported by the Danish authors cited, were in patients with diseases of the central nervous system (particularly post encephalitic parkinsonism, syphilis, tumors syringomyelia, et) and were regarded, along with other cutaneous changes (hypertrichosis, eczema, lichenified prurigo with pseudosegmental distribution) as an expression of central nervous s tem m of ement especially of the mesencephalon The fi t case reported France was by C Simon n 1945 Since 1949 bout 20 cases ha e been observed in Lyons includi g the autho 13

Michel therefore believes that this pigmented l ne on the

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forehead is not so rare as the Danish author thought. The finding predominates in women and occurs under varied etiologic conditions; it is not always possible to determine whether or not these are coincidental. Among conditions noted in the patients studied were Parkinson's disease, syphi-

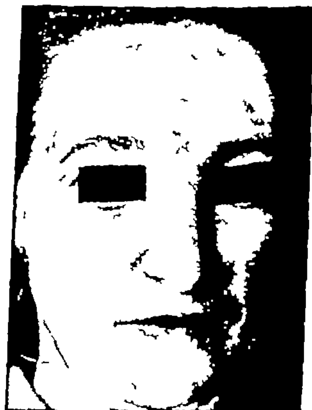


Fig. 25.—Linea fusca, associated with old freckles. (Courtesy of Michel, P. J.: Ann. dermat. et syph. 65: 509-21, Sept.-Oct. 1938.)

lis with and without involvement of the nervous system, enteropathy, pregnancy, goiter and arthritis. Five of the 10 women related the pigmentation to a previous pregnancy; 3 said that the frontal line represented the remains of a chloasma.

These facts suggest that the anomalous pigmentation may have an endocrine-sympathetic origin in an imbalance of hormones (hypophysoadrenal or sexual) and vitamins (C, PP, B_6). Regardless of whether or not this hypothesis is cor

ect, t seems certain that the original concepts as to cause pathogenesis and diagnostic alue of the forehead line should be reconsidered in the light of the observations here presented.

The typical lin or band is about 1 cm wide, with varying tensity of pigmentation which is sometimes slightly lighter toward the center of th face and forms a loop design that may be more or less pronounced (Fig 25) Sometimes the pigmented line is prolonged toward the masseteric region, but t is always parallel to the scalp There i always a light trip between the hairline and the pigmented band.

Melanoderma of Bright s Disease Two New Cases were observed by H Thiers Pierre P Ravault, Daniel Colomb and Edouard Lejeune[3] (Lyons France)

Woman, 60, was admitted for treatment of chronic azotemic nephritis At age 37 she had had acute nephriti with albuminuria and edema but without hypertension, from which she had recovered in 2 months. Four months before admission, marked asthenia developed, accompanied by headache, anorexia, nausea and omiting dyspnea on exertion and edema of the legs. Her family physician then found nephritis with hypertension (240/130) and azotemia (0.90 Gm.) Despite treatment, the condition progressed, and examination on admission revealed severe clinical, laboratory and ocular signs of chronic nephritis. Blood urea anged from 1 5 to 4.5 Gm

The patient exhibited generalized pigmentation which was more prominent on exposed parts. The face was dull gray without pigmentation of the mucosa. Forearms and legs were of darker (dead leaf) olor limited to exposed part Nipples and genitalia were normally pigmented Also present wa diffuse cutaneous atrophy of the senile type.

Skin biopsy showed marked thinning of the epidermis which lacked papillae and consisted of only 3-4 cellular layers, with disappearance of the granula layer The dermis was slightly trophic, but without infiltration or ascular lesions the only change was general increase of pigment in the basal layer of the epidermis. Melanin stains confirmed the existence of an abnormal quantity of pigment which was seen in all layer of the epidermis including the corneal layers. No pigment as found in the dermi

Skin finding a w ma 52, were imilar with melanin in all la ers f the epiderm t was most marked n the basal la er Also a moder te mount of pigment wa found n the derm either free o within the cytoplasm of small histiocytes

The exact mechan sm of m lanoderma in Bright d sease

(3) Ann. dermat. et syph. 267 277 May June, 1948

forehead is not so rare as the Danish authors thought. The finding predominates *in women and occurs under varied eti*ologic condition it is not always possible to determine whether or not these are coincidental Among condition noted in the patients studied were Parkinson s disease syphi



Fig. 25 —Linea f sca, associated ith old freckles (Courtes f Michel, P J Ann. dermat et syph 85 509 521 Sept Oct 1958)

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Cutaneous Manifestations of Chediak Higashi Syndrome are specific and definit., according to Dagoberto O Pierini and Jorge Abulafia (Buenos Aire) Only 3 cases of this hered tary malady ha e been reported previously The ash gray color of the hair the slate-colored skin in exposed re gions and the gigantic granules of melanin in histopathologic section con titute a dermatologic triad which suggests the diagnosis This triad, with granulation of leukocytes (neutrophils and monocytes especially) and ocular fu di haracteristic of the albino are the most con tant ign of th Chediak Higash yndrom

Boy had ash gray hair at birth, and at age 9 months slate gray pots ppeared on the cheeks later similar patches developed on the fore head and extremities. The skin remained smooth without notable change thickness and elasticity Distribution of pigmented areas, with sparing of the periorbital and peribuccal regions and a band bout 5 mm. wide below the hairline, gave the face a peculiar mask like appearance.

From the first months of life, the child had repeated febrile illnesses, secondary t sore throat or enterocolitis at times but often w thout evident cause At age 18 months, a febrile attack associated w th mucopurulent rhinopharyngitis wa accompanied by adenopathy (etroauricular and inguinal) hepatosplenomegaly abdominal distention, poor general condition, pallor and marked photophobia Blood studies suggested the presence f leukemia and the patient was hospitalized for more detailed clinical study The ocular fundi were similar to those seen in albinos. Hematologic study revealed marked anemia (7 45 Gm /100 ml. hemoglobin) thrombopenia, neutropenia (8-12%) and lymphocytosis (80-90%) Cytoplasmic granulations were demonstrated in the neutrophils of the peripheral blood and in the myeloid cells of the bone marrow The peroxidase reaction was at first negative but showed the characteristic staining later

Skin biops showed loose hyperkeratosis in the epidermis with large granules of melanin in clumps. The granula layer was represented only by isolated cells. The malpighian layer was of normal thickness ith slight development of interpapillary crests. Apical poles of basal cell and of some mucosal elements were occupied by accumulations of melanin granules of unequal size, some extremely large. The hypodermis was normal. In some hair bulbs and in the cortical zone of ha roots, gigantic granules of melani were seen.

After bout 2 months, the patient showed improvement on antibiotic treatment and repeated hol blood tran fusions. Later he had chickenpox and measles He was much improved at the end of 5 months. During the next 3 years, he continued to show susceptibility to infections.

At age 4½ his general health deteriorated suddenly with reappearance of marked hepatosplenomegaly and recurrent febrile episodes.

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is still to be elucidated According to Becher's theory the abnormal pigmentation is due to accumulation in the skin of aromatic substances of intestinal origin becoming brown under the influence of solar rays and retained in excess as a result of the chronic nephritis. The xanthoprotein reaction of Becher and Jolles reaction measuring retention of indican were both strongly positive in these 2 patients. These findings represent only part of the problem and much still remains unknown e pecially changes in activity of tyrosinase and in the cycle of the melano-stimulating hormone

Skin Manifestations of Chronic Acidosis. Edwin (Olmstead and John H Lunseth[4] (Marquette Univ) present 5 cases of dermatitis associated with chronic renal disease All 5 patients showed thickening of the skin dryness scaling and loss of body hair particularly over the extremities. The most striking histologic finding was an increase in elastin fibers in the papillary layer of the skin and in the perifollicular regions which seemed to be correlated with the degree and duration of the acido is The fibrous tissue wa not appreciably increa ed in any of these areas. The degree of kin involvement clinically and pathologically was more closely related to the degree and duration of the acido i than to any other single chemical abnormality of the erum Skin changes occurred in the presence of normal nonprotein nitrogen chloride and total serum osmolarity

The authors conclude that the ela tosi in these patients resulted from conversion of nonelastin (for the most part collagen) to elastin in the papillary and perifollicular regions the conver ion being in some way due to acidosis. In favor of such a conver ion is the close chemical imilarity between collagen and elastin and the fact that collagen has been converted into ela tin in vitro by treatment with 1% sodium m periodate at pH 5 and with dilute acid or alkali

Clinical improvement of the kin lesi n with lo of itching and regrowth of hair occurred in 2 patient with chronic acidosis treated with sodium bicarbonate for 8 and 5 month In 1 case repeat biop y after treatment how ed normal histology

Skin changes similar to tho e seen in patients with chr ni acidosis did not occur in a patient with hyperchloremia, hypernatremia and hyperosmolarity of 7 years duration

(4) A.M.A. Arch Dermat 77 304-313 March, 1 5

Canizares Fabio Uribe J ramillo nd Francisco Kerdel Vegas The reaction was observed frequently n these coun tri where commercial preparation contain ng monoben z l ether of hydroqu none may be obtained over the counter w thout prescription. Most cases occurred in patients with a h ghl pigmented skin. Some were possibly Cauca ian bru n ttes but most presented ev dence of mixtures of Cauca ian Indian and/or Negro blood.

I all cases the sequen of e ent wa a follows. Th pa tient applied a preparation containing monobenzyl ether of h droquinone t th face for 2 week to a few months An acute contact dermatiti de eloped on the affected areas. It u ually subs ded f treatment w l scont nued and soothing med cation pplied In ra e cases ther w no h tory f dermatitis, though some pat ents had pruritus, which may ha ndicated a ubclin cal derm titi Two week to ? months after disappearance f the c ntact derm titi area t depigmentation mi ed w th area f h perpigment tion dev loped the area pre iou ly affected and on their pe riphery Lesion at a d tance, u h a on arms, bdomen d legs were also present n some patients. I m t cases n e planation could be offered for the location of th d tant lesion The dyschromia alway consi ted of r und or o al macul s, and no tance of li ear o ngular hapes wa bserved

F olut on of the lesion w ha cteri tic They p ead a d extended for 1 2 month and then were stationary Some times there wa pon tane u regression If the lesions wer t eated w th m tho salen hyperpigmentation ppeared m re nsi tentl th qui ed leukoderma than when iginal patch f til g wer t eated with the same med tion Severer rea tion to th med cation were found in th type of leukom lanoderma tha in true vitiligo

Most patient had ppl ed 20% concentrati n of mono-benzyl ether of hydroquinone obtained n a commercial prep-rat on Some pat ent treated by d rmatologists had used p eparation contain ng 2 10% in an ointment base or in l hol tincture

Th uthors conclud that treatment of lesions, uch hloasma n patient with a naturally hyperpigmented skin with preparations containing monobenzyl ether of hydro-

M A Arch Dermat 77 220-223, February 1958

Three months later jaundice developed and he was rehospitalized. There was marked anemia (8.77 Gm./100 ml. hemoglobin) leukopenia (3,000 white cells) neutropenia (12%) and lymphocytosis (80%). Five months later the general downhill course was aggravated by pleurisy. A month later generalized convulsions were followed by amaurosis, which was controlled after administration of chlorpromazine for a few days. The general state deteriorated slowly and abdominal distention increased. Neurologic signs included headache, transitory pareses, tremors and emotional instability. The EEG revealed marked paroxysmal dysrhythmia with disorganization of bioelectric activity but no focal signs. The patient died about a month after his 5th birthday. There was no autopsy.

Incontinentia Pigmenti: Report of a Family. Incontinentia pigmenti usually begins in early childhood as a series of linear and grouped vesicles on an erythematous base which when ruptured tend to become impetiginized. These may disappear and recur for weeks or months gradually giving way to an intermediate temporary stage of linear verrucous lesions or the vesicles may lead directly to the third or pigment stage characterized by a reticulated pattern of pigmented macules, whorls, lines and patches. Many years later in some patients a final stage may occur in which the lesions fade leaving no blemishes or slightly atrophic, lightly depigmented areas to mark the sites. Many cases are associated with mild to severe ecto- and mesodermal defects.

Sophocles D. Marty, H. Bernard Bechtel and Clayton E. Wood[6] (Indianapolis Gen'l Hosp.) report a family tree in which all the female members (5) for three generations showed the cutaneous lesions of incontinentia pigmenti. These patients tend to support the sex limited mode of inheritance. One male member of the second generation had developmental defects without skin lesions. Because no defects were found in any other members it remains conjecture whether these defects were associated with incontinentia pigmenti or were mere coincidence. The fourth stage is often overlooked. Two of the present patients are in this stage; 2 others passed through this stage and their condition stabilized with minimal pigmentation. The fourth stage makes acquisition of detailed family histories difficult because patients tend to forget skin blemishes of their childhood.

Leukomelanoderma Subsequent to Application of Monobenzyl Ether of Hydroquinone: *Vitiligoid Reaction Observed in Colombia and Venezuela* is described by Orlando

(6) A.M.A. Arch. Dermat. 78:407-411, November, 1958.

tio (seropapule) If such an early lesion is scratched off the epidermis is usually mis ng n the central areas.

Chron papular urticaria has to be liff rentiated fr m lichen prurigo and urticaria.

Treatment depend on the patient age Women in the climacteric, or menopause, may be treated with corpus lute um. During pregnancy local treatment i sufficient since the disease usually subsides after pregnancy Local therapy con sists mainly f antihistamines. Occasionally good results were seen after infiltration of the subcutaneous tis ues of the ffected area with Sympocaine[a] which is a procaine deriva tive with depot effect. Under this treatment even distant lesions seemed to disappear

► [Much remains to be learned about chronic papular urticaria, acne urticata and other pruritic papulourticarial eruptions of the face, upper chest and back Each ha been described under various names Some seem to be acneiform eruptions in individuals highly susceptible to itching who scratch and pick the lesions Others are associated ith polycythemia, leukemia, drug and light sensitivity and hormonal disturbances or are lesion locally produced by cosmetics —Eds]

Further Observations on So-called Lichen Vidal Urticat us. A Greither and H Tritsch[a] (Un v of Heidelberg) tud ed 17 women and 7 men w th lichen Vidal urticatus. The women were p egnant, climacteric preclimacteric or showed other distu bance of sex hormones Localization of the skin lesion varied in some patient the trunk and l mbs wer multaneously affected in others the trunk wa n t affected (Fig 26) whereas in another group the papules h wed d tribution milar t acne vulgaris. Notwith tanding the differences in local zation the linical appearance wa rather mila m all th patients scrat hed flat nod les n ll covered with cru t were pread widely and there were man pigmented scar f sim lar ize Severe it h ng was not diffuse but w limited to the papules, subsiding as soon as the lesion were dest oyed by scratchi g In se eral patients lichen Vidal urticatus and lichen hronicu V dal were present together

De lopment f lichen Vidal urticatu begi with edema i the upper corium accompanied by acanthotic w den ng of the epidermis The edematous welling of the connecti e t ues combined w th further acanthotic widening and hy perkeratosis f the upper corium will lead to the fully de loped mi ed papules f lichen hronicus Vidal All other

[a] Hautarzt 9 198 203, May 1958

quinone is hazardous. The leukomelanoderma which develops in many cases is cosmetically more objectionable than the original hyperpigmentation.

► [Monobenzyl ether of hydroquinone may produce excessive depigmentation, especially in colored persons even when used under careful medical supervision. However, apparently it does not produce these leukomelanodermic changes in these patients except after engendering a contact (allergic?) dermatitis. —Eds.]

Urticaria Papulosa Chronica. From their studies on 11 women and 1 man aged 23-53, O. Braun-Falco and U. Mirlicktedt (Johannes Gutenberg Univ.) learned that this condition is a well defined clinical entity. It usually starts with small nodules on a healthy skin. The intense itching accompanying the nodules subsides as soon as the lesions are scratched off. The typical skin changes consist of eroded, blood-crust-covered pinhead- to lentil-sized eruptions, and of hyperpigmented or pale atrophic areas of former healed eruptions. The lesions do not form groups or coalesce. Secondary infections are rare. Involvement of the oral mucosa was not observed.

The disease affects mostly women. Of the 11 women all but 2 had sex hormone disturbances. The skin changes subsided after hormonal treatment or delivery. The only man in the study group had had one of his testes removed before the skin erupted; the other testis was atrophic. These observations support the assumption that chronic papular urticaria is due to hormonal dysfunction. However, it was not possible to identify the actual dysfunction responsible for the disease.

The histologic picture depends on the stage of the disease. In fresh lesions the epidermis is somewhat widened. Often there is some tendency to proliferative hyperkeratosis leading to widening of the stratum granulosum. Inter- and intracellular edema (vacuolation) is visible in the deeper layers of the stratum spinosum. The dermal changes affect mostly the papillary bodies and superficial parts of the reticulum layer. The edematous connective tissues contain particularly widened vessels surrounded by loose lymphocytic and eosinophilic infiltrations. This perivascular infiltration extends into the area of the sweat glands. The latter are not affected. In the disease course cavities filled with blood serum, leukocytes and possibly erythrocytes develop in the upper parts of the epidermis leading to typical vesicle forma-

(8) Hautarzt 8:334-340, December, 1957

Basi changes i ene urticata con i t of it ten i red millet-si ed urticarial papules or nodules that ar crowned b a hardly isible bli te and may be urroun led by an in flammatory halo Intensi e tching characteri tic and i essentially limited to the primary lesions and their v cinity Hi t logically the acne urticata lesion re characteri ed n th beginn ng by edema of the cutis late also of the epider mi with sub- nd i traepidermal vesicle formation an l by

ig 37 Acne excoriee des jeunes filles (Brocq) Besides many comedos on for head ... there are several well circumscribed excoriations in lateral frontal areas Hyperpigmentation ... (Courtesy of Saalfeld, K Hautarzt ... December 1937)

necros s of the epidermis and papillary bodie without pri mary n ol ement of the foll les Acne-like changes a absent

Neurot c excoriation lead to corr tion n tl fac lik the abo e two entit es, but may also be found in any other areas within reach of th scratching hand. There are no basic pathologic ha ges The cause fo scratch ng l es the ps hi abnormal ty (hy teria) of the patient

The author believes that ther close relation between n rticata and rt aria papulosa chronica. Acne urticata and acne excoriée houl l be differentiated from acn necrot ca Boeck Th papulonecrotic lesions, good therapeutic re l onse to leukomycin n l residual riol form car a t pical f acne necrotica.

I treatment of acne urticata, if correction of basic medical (h rmonal) or gynecologic abnormal ties f il sedation and

features such as the subcorneal vesicles necrotic changes of the epidermis crust formation and hemorrhages are secondary and due to scratching

In differential diagnosis lichen urticaria and prurigo must be considered The common feature with lichen is the similarity of the papule However lichen Vidal urticatus does not cause lichenification of the skin Clinically lichen Vidal urticatus has not much in common with urticaria Histo-

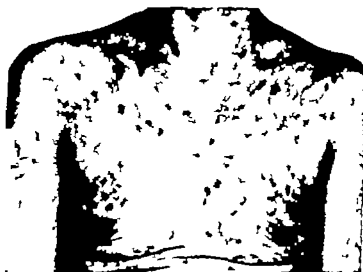


Fig 26. Trunk more involved than limbs (Courtesy of Crether A., and Trauch, H Hautarzt 9 198-204, May 1958.)

logically edema is prominent in the connective tissues which in urticaria is not accompanied by acanthotic widening of the epithelium In prurigo nodularis and lichen Vidal urticatus itching is in the foreground but in the latter the individual lesions seem smaller than in prurigo nodularis

Differentiation between Acne Urticata (Kaposi) Acne Excoriée des Jeunes Filles (Brocq) and Neurotic Excoriations is analyzed by K Salfed[1] (Johannes Gutenberg Univ) Acne excoriée and acne urticata are two well-defined completely separate entities that have only their name in common In acne excoriee (Fig 27) which is limited to the face and affects almost exclusively females aged 16-24 the patient is stimulated by the basic changes of acne papules and comedos to scratch the face Itching is not more pronounced than in acne vulgaris

(1) Hautarzt 8 546-549 December 1957

Basic changes in acne urticata con t of inten i e red millet-si ed urticarial papules or nodules that are crowned b a hardly visible blister and may be surrounded by an inflammatory halo. Inten ive it hing i characteri tic and i essentially limited t the primary lesion and their vicinity Histologically the acne urticata lesion are characterized in the beginning by edema f th cutis, later also of th epider m w th sub- and intraepidermal vesicle formation nd b



ig 22 Acne excoriee des jeunes filles (Brocq). Besides many comedos on forehead above area, there are several well visualized excoriations in lateral frontal areas. Hyperpigmentation normal) (Courtesy of Saifeld, K Hautarzt 8 346-349 December 1957)

ecrosis f the epidermis and papillary bodies without pri ma ol ement f the f llicles Acne-l k cha g are abse t

Neurotic excoriation lead to excoriations in the fac l k the above tw entities but may also be f und n any ther area w th reach f the scrat hi g ha d There ar no ba ic pathologic changes The cause for scratch ng l es in th ps ch abnormality (h teria) of th patient.

The author believes that ther i lose relation between ne rticata and urticaria papulosa chronica. Acne urt ta and ne corn‑ée bould be differentiated from acn necrot ica Boeck The papulonecrotic lesions, good therapeutic ponse to leukomycin and residual variol f rm sca e t pical of acne necrot ca

In treatment of acne urticata if correction of basic medical (hormonal) or gynecologic abnormal t es fail sedation nd

antiurticarial care are in the foreground. Treatment of acne excoriée is the same as in acne vulgaris.

► [To the uninitiated and those not specially trained in dermatology the differential diagnosis of the various acneform eruptions of the face may present many difficulties. It is only through accurate diagnosis that appropriate therapy can be planned.—Eds.]

Acne Urticata Polycythemica: Report of Case is presented by Donald L. Baxter and James H. Lockwood[2] (US Naval Hosp., Philadelphia). This is the 15th case reported in the literature and the 4th in which oxidase granules were demonstrated in the cellular infiltrate.

White man, 66, had a skin eruption for about 3 months. The eruption was generalized, sparing only the face, palms and soles and partially sparing the middorsal back. The lesions consisted of erythematous macules, papules, excoriations, hemorrhagic crusted papules, pure vesicles and bullae on normal appearing skin and pustules surmounting papules. There was superficial scarring at the site of former lesions. On both feet there were scattered bullae and bloody ulcerations at the sites of former bullae. An ulcer on the dorsum of the left great toe was secondarily infected.

The patient's complexion was ruddy, with injection of the conjunctivas and mucous membranes. The lower extremities were of a dusky violaceous h[illegible] with [illegible] superfic[illegible] when dependent. Re[illegible] 24.4 Gm. re[illegible] vol.%. The [illegible] men[illegible] neutroph[illegible] 5% eosino[illegible] of 8,820 [illegible] led hyper[illegible] revealed prominence of the perivascular markings and hilar vasculature with borderline enlargement of the cardiac silhouette and left ventricular prominence consistent with the clinical finding of polycythemia.

After 2½ months' observation and trial, the eruption subsided without treatment. Treatment of the polycythemia was then started. The patient was bled a total of 3,[illegible]55 cc. in about 500-cc. increments during 3 weeks. Though there was marked improvement in the ruddy violaceous hue of the skin, new erythematous urticate papules started to appear after 2,230 cc. blood had been removed. The recurrent eruption subsided during the next 2 weeks with continued phlebotomy.

Histologic examination of an urticate papule revealed a cellular infiltrate of eosinophils, polymorphonuclear leukocytes and mononuclear cells throughout the upper dermis and papillae and a light infiltrate deep in the corium. After a saturated solution of benzidine dihydrochloride in 0.2% hydrogen peroxide and 40% ethyl alcohol was injected into a papule according to the technic of Weidman and Klauder, peroxidase granules were demonstrated in the macrophages scattered throughout the dermis and in the eosinophils, which were so heavily

(2) A.M.A. Arch. Dermat. 78:325-329, September, 1958.

laden as to be obscured by brown pigment in vitally stained specimens, whereas they were numerous in other biopsy specimens.

Further study is necessary to ascertain whether the peroxidase reaction is a constant finding in acne urticata polycythemica and to determine the significance of the peroxidase-positive macrophages found in the cellular infiltrate.

► [The clinical manifestations of polycythemia are many and varied. The possibility of its occurrence should be considered in patients, particularly in men who have a florid, flushed appearance or in those who present bizarre urticarial lesions.—Eds.]

Eczematid-like Purpura. M. Binazzi and A. F. Fiorzi[3] (Univ. of Perugia) report 2 cases.

Case 1.—Man, 45, in good general condition, had noted 6 years before a brownish red lesion, painless and nonpruriginous, about 5 cm. in diameter on the inner malleolus of the left leg. This remained unchanged until 10 months before observation, when a punctiform purpuric lesion appeared at the edges of the initial lesion, which at this time regressed. Similar lesions appeared on the same leg, the other leg, the thighs and within 40 days on the trunk, mainly the waist and gluteal region. Itching, intense at the outset and during the period of dissemination, decreased as the lesions tended to form irregular groups in reticular distribution, with superficial lichenification and scaling, in which the purpuric feature tended to lessen. Purpuric lesions were noted in the oral mucosa and there were focal infections of the tonsil and teeth. The tourniquet and capillary fragility tests gave no significant results. Laboratory findings were negative and the histologic findings conformed to those described by Doucas and Kapetanakis. Quick but transitory benefits were derived from prednisolone therapy, but wide-spectrum antibiotics were ineffective.

Case 2.—Man, 68, father of patient in Case 1, with whom he lived, in fair health, although he had had a history of chronic gastritis since age 40 and of nervous breakdowns. Red, itchy, at times exudative lesions had appeared in the presacral region and inner malleolus of the right leg 3 years before and had receded spontaneously 4 months before observation. Two months later small puncta and red spots developed on the legs and gradually on the thighs, abdomen, shoulders and forearms, always accompanied by pruritus, which was especially intense at night. The course of the dermatitis, and the clinical, laboratory and histologic findings, as well as the therapy and its results, were similar to those in Case 1.

The literature suggests that eczematid-like purpura is an epidermitis probably secondary to a process of acute recurring capillaritis. The authors advance the hypothesis that the condition probably has an infectious etiology and pathogenesis of microbic type in which both capillaries and epithelial tissue may be attacked. The results of prednisolone and antibiotic therapy seem to support this hypothesis. A

[3] Gior. ital. dermat. 99:127-43, Mar.-Apr. 1958.

virus etiology i excluded in view of the good general condition of both patients the normal protein picture and the absence of hepatic and medullary alteration The p ssibility of its being a genodermato i i al o excluded

Schönlein Type Exanthema with Peculiar Disturbance of Blood Clot Retraction was observed by C W Korting I K *Beller and C Koppel*[4] (*Univ of Tubingen*) in the ll n ing ca e

Man 48 had diarrhea followed a few weeks later by a rash covering the whole body Two weeks later slight fever and moderate joint

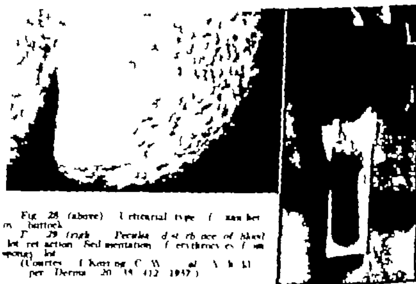


Fig 28 (above) Urticarial type f xan hem on buttock
F 29 (right) Peculiar d st rb nce of blood lot ret action Sed mentation f erythrocy es f om sponge) lot
(Courtesy f Korting C W al A h kl per Derma 20 18 412 1957)

symptom I eloped Ph ical xa n n t n revealed a somewhat enlarged l ver The k n x other affected pr ctically the entire b l except the face neck anteri r and p steri r su f ces of the chest and upper part f the scr tum Th n bode a p o nently in ol ed The kin changes vere composed partly f pinp nt ized hemorrhages similar to those seen n scurvy a d Werlh f l sease and partl of lentil-size l light red ar a f them n ere slightly elevated, as in urticaria (*Fig 28*) a d he ed aft the edema h d disappeared pinpoint ized hemorrl ag w th n the erythema seen in nonthrombopenic (Schonlein) purpu The e no hema toma Pinpoint sized hemorrhages were l d sen I i the l I mucosa on the lips and back of the tongue Dur ng the 3d l sp t l eek hematuria appeared and the blood pres ur h l m rm l bet e to 180/120 mm Hg

The skin biopsy pecimen howed the t i l i ture f Schonlein purpura The most strik ng lal orat ry h l g w the d turl nce

(4) Arch klin exper Dermat 20 44 2

blood clot retraction (Fig 29) The routine coagulation test (heparin tolerance, Quick's test, recalcification time) showed normal alues There was a compensated serum disturbance due t insign fi cantly diminished factor IX. Electron microscopic tudies did not show any morphologic changes in the thrombocytes f the patient. H wever ther was a tendency to increased adhesion and concentra tion of thrombocytes into giant clumps which might ha hindered the development of an organized fibrin structure leading to d sturbed clot retraction as is true when agglutination is absent.

I th patient there was probably some etiologic relation between the ski exanthem and disturbance in the clot retraction mechanism.

Hyperergic Panvasculitis with Multiple, Symmetrical Skin and Bone Gangrene is discussed by A. Matras[3] (City Hosp Vienna Lainz) The skin lesions in angi tis vary As



Fig 30 Symmetrically localized superficial skin necrosis about weeks after onset of disease (Courtesy of Matras A Arch klin exper Dermat 207 32 540, 958

periarteritis nodosa, there is mult ple circumscribed nod la th kening of muscular type the small and medium ed arteries f one or several organ system includ ng the sk The k manifestations of periarteritis nodosa may be nodula purpura l ke gangrenous. The d agnosi i f cil tated b nodula densities the ubcuti Pan ascul ti led k d bon gangrene in th case described.

Th following measles at age 5 had attack of wollen joints, fever nd) thema multiforme-like ski eruptions whenever some purulent th n a er extracted The eruptions finally developed into exten- necrotic gangrenous skin changes They were symmetrically lo- alized over extens area of the upper and lower extremities (Fig 30) and over the buttock and sacral egion Besides, there

ch klin exper Dermat 207 521 540

were circumscribed necrotic areas on the lips, tips of the nose and tongue, buccal mucosa and ears.

Treatment with antibiotics, sulfonamides, ACTH and cortisone resulted in temporary improvement to the patient. Following complete mummification of the necrotic skin areas, the end and middle phalanges of all fingers fell off These phalanges and the urine contained much porphyrin. Severe peritonitis due to perforating ulcerations of the stomach and bowels led to death 2½ years after onset of the disease.

Histologically there were severe vascular changes in the skin and bowel walls, consisting of fibrinoid necrosis of the media and leukocytic infiltration in the vascular wall and occasionally also thrombus formation

It is believed the patient had the cutaneous gangrenous form of hyperergic panvasculitis due to an infectious toxic process

Trisymptomatic Syndrome of Gougerot (Dermal Nodular Allergids) Is It a Lesser Form of Periarteritis Nodosa? This question is discussed by P Témime and A. Rodde[6] (La Timone Hosp Marseille France) based on the following case

Man, 47 had a history of alcoholism, malaria and serum sickness after diphtheria. His present illness began in August 1956, with a poor general condition fever and malaise, followed by eruption of cutaneous nodules on the legs and arthralgia with swelling of the fingers wrists, knees and ankles, which responded to treatment with Alencyl Later there was parallel progression of cutaneous and joint manifestations of longer duration which required hospitalization in October 1956, and corticotherapy In May 1957 there were polymorphous cutaneous eruptions on the arms and legs, consisting of papules, purpuric nodules and pustules pruritus and enlarged lymph nodes. The temperature subsided under Butazolidin® treatment and the joint pain lessened somewhat In September 1957 examination showed urticarial plaques dermal nodules pigmented macules (scars of previous nodules) significant adenopathy in inguinal axillary and epitrochlear glands. Antiallergic and antihistaminic treatment was continued, but the urticarial plaques and skin nodules persisted. Some were purpuric and painful Antiallergic treatment with vitamins for capillary protection and then deltahydrocortisone in large doses were given Since November 1957 the cutaneous and joint symptoms regressed strikingly but manifestation of arteritis increased with necrotic ulcers of the 2d and 3d toes and absence of pulsation in the leg

The authors believe that the lesions in this case were not merely coincidental and that Gougerot's syndrome is a minor form of periarteritis nodosa further that other syndromes including anaphylactoid purpura vasculitis of hypersensitivity granulomatous vascular allergid H rt n

(6) Rev lyon. méd. 439-434 March 1958

yndrom nodular vasculitis and Still s disease, may be related. In all these conditions there are vascular changes and flammatory infiltrates in the skin and also in the v scera and lymph nodes. In all the etiologic factor appears to be allergy with resulting arteriol t s or necrotic arteritis, and they often respond to the same treatment, i.e. corticotherapy Whether the changes produced are cutaneous or visceral, or both, depends on the inten ity of the etiologic process, pre di pos tion—acqu red or spontaneous—and localization (cap llaries, arterioles, arteries of small or averag caliber) Anatomico-clin cal manifestations may be of various types benign acute with a ingle attack, as in anaphylactoid pur pura hronic recurring as n dermal nodular allergids severe (allergic granulomatosis) or lethal as in periarteritis nodosa of low or rapid progres ion. Polymorphism and dif fering courses of these varion affections deri e from the localization and ariable intensity of the pathologic p ocess.

Hypodermic Vascular Allergids B Duperrat and J Mon fort (Paris) exam ned the evidence for and against the al lergic origin of varion lesions, ncluding Gougerot s nodular llergids, periarteritis nodosa, nodular vascul tis Bazin s erythema d ratum erythema nodosum, migrant thrombophl b ti and panniculi ti (Weber-Chri tian disease) Based on a ew of Montgomery s d scription of nodular vas cul tis 25 cases of this type were studied. All patients were women aged 23-68 (a erage 43) Only 2 had a history of asthma or eczema. The illness began with heaviness in the leg a d nexplained asthenia, sometimes swelling of the ankles, followed by sudden appearance of nodules, often within 4 hours Only 2 patients had varices. The course was subacut often lasting for years and each attack (often sea sonal in Mar h to April) was preceded by asthenia and leg pain

I estigation f the focal sepsi revealed 5 pat ent w th hi t ry of pulmonary tuberculos s, 2 heumatic carditis, 8 f muclea gen tal suppuration 5 infection of digest e t act and ppendicitis, 2 repeated anginas and 4 dental com pl tion Some patients had had several nfections In 5 ther wa no history of focal seps In 3 the first attack curred d ing pregnan y No bacteria were solated from the material obtained t biopsy or punctu e of the nodules.

Ann dermat et syph 3 30:4 July Aug 1953

Tests for bacterial allergy showed that 5 patients had extreme hypersensitivity to tuberculin and seemed to belong to the group with Bazin s erythema induratum 4 had selective hypersensitivity to streptococci 2 to staphylococci and 1 to staphylococci plus Bacillus coli Thirteen showed no specific hypersensitivity In all patients with allergic sensitivity hypergammaglobulinemia was found. The total globulins were often 75-80 Gm and the gamma globulin was usually over 17% in 5 it was over 20% In some cases there was hyperfolliculinuria. The etiology does not appear to be uniform but some cases definitely seem to have an allergic origin

The authors conclude that in apparently sensitized patients there is a whole gamut of lesions some known for a century e.g., Bazin s erythema induratum others for a long time e.g erythema nodosum and others more recently described. All have in common that (1) nodular lesions may appear and disappear rather rapidly without necessarily leading to ulceration (2) the lesions have a pathologic vessel at the center (3) the phenomena of necrosis are frequent and (4) the granulomatous reaction is secondary These conditions form an uninterrupted series of lesions from the most benign to the most serious which present at the beginning serious prognostic difficulties The allergic nature of these lesions i evident in Gougerot s dermic nodules and in some cases of nodular vasculitis it is very probable in periarteritis nodosa probable in many cases of erythema n dc um and of migrant thrombophlebitis

This idea is important because it permits an orientation of future work with regard to therapy — till uncertain—in these pathologic conditions which are increasing in daily practice

Postphlebitic Syndrome con ist f progre ive develop ment of deep venous insufficiency and it complications It i caused by deep venous thrombosis in the pelvic veins or in those of the lower extremitie This lead to edema develop ment of collateral vein pigmentati n indurati n pecially above the medial malleolus a characteri tic dermatitis and ulcer The incidence of postphlebitic yndrome i difficult to estimate Though many patient give a clearcut hi tory f a deep venous thrombosis after childbirth injury operation infectious disease or prolonged immobili ation as many have no recollection of such a vascular accident in the vein

\ charleyhorse after bowling an ankle strain or a "ruptured muscle treated by taping is often the beginn ng of a series of events leading to serious disability according to Geza de T kat (Univ of Illinois)

Recanalization of the thrombus destroys the alves and leads to postural regurgitation. Incompetent commun cat ng ei s freely tran mit, from the deep to the superficial eins the sudden rises of venous pressure during coughing lifting tra ning and sneezing Symptoms follow in a defi n te sequence, from those f the nitial thrombosis and subsequent bouts of periphleb tis through the stages of edema, varicosities, pigmentation dermatitis and induration to that of ulcer To prevent the long lasting recurrent disabilities seen in the later stages intensive treatment of the earlier tages is necessary

In the tage of incip ent deep thrombosis there calf pa n c ano on dependency and some distention of the dorsal vein of the foot. There may be minimal or no edema. Infla tion of a blood pressure cuff on the affected limb to 80-100 mm Hg produces severe pain. Dorsiflexion of the foot kes pa th flexor muscles of the calf or in the popliteal fo sa n about half the cases The affected calf frequently w rmer Treatment con ists of hospitalization with the foot of the bed levated and dministration f heparin for 2 weeks. The patient i ambulatory in 3 days nd wears an elastic t cking t r 6-10 weeks

In th later tages recurrent periphlebitis s treated by short int rval f ntense l ation of the limb edema is controlled by elastic support and varicosities resulting from val \ lar sufficiency re treated by ligation and stripping

W t d es ing f alum um subacetate solution, Vioform cam and h drocortisone tment have been found to be seful in treatment of dermatiti of the leg Early xcision of plaques of postphlebitis induration is advocated. Whenever possible the skin i sa ed, but t must be removed if badly damaged In the early tages f ulceration, ambulatory treat ment with a gly erin-gelatin cast may be succes ful After the lcer i healed the induration i excised, w th without grafti g indicated Palpation of the skin and it t xture trophy and obvious vulnerabil ty are the best guides in de ding wh ther or not the skin co ering the nduration

J M A 164 114 947 Aug 24, 1957

Tests for bacterial allergy showed that 5 patients had extreme hypersensitivity to tuberculin and seemed to belong to the group with Bazin's erythema induratum 4 had selective hypersensitivity to streptococci 2 to staphylococci and 1 to staphylococci plus Bacillus coli Thirteen showed no specific hypersensitivity In all patients with allergic sensitivity hypergammaglobulinemia was found. The total globulins were often 75-80 Gm and the gamma globulin was usually over 17% in 5 it was over 20% In some cases there was hyperfolliculinuria. The etiology does not appear to be uniform but some cases definitely seem to have an allergic origin

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Postphlebitic Syndrome consists of progressive development of deep venous insufficiency and its complications It is caused by deep venous thrombosis in the pelvic veins or in those of the lower extremities This leads to edema development of collateral veins pigmentation induration especially above the medial malleolus a characteristic dermatitis and ulcer The incidence of postphlebitic syndrome is difficult to estimate. Though many patients give a clearcut history of a deep venous thrombosis after childbirth injury operation infectious diseases or prolonged immobilization as many have no recollection of such a vascular accident in the vein

Arilus cristatus is a reduviid of the order Hemiptera. All Hemiptera have piercing mouth parts and are likely to be dangerous when handled. The wing structure of th s group differentiates them from the Coleoptera, which are generally mechanically harmless beetles. The distinctive feature characterizing the winged species of Hemiptera is the structure of their outer pair of wings, which are thickened in the proximal portion and are membranous in the distal portion with verlapping of the wing tips Typical beetles differ in that the outer pair of wings a e entirely chitinized, hard and



Fig 31.—Arilus cristatus, showing cogwheel-like crest, elongated head and stout proboscis (Courtesy of Smith, F D et al A.M.A. Arch Dermat. 77:324-330, March, 1958)

opaque, meet n straight line down the back nd serve as wing covers for the membranous pair of wings underneath.

The present case substantiates the generally a cepted opinio that, a ide from pain, serious or prolonged ffects from the bites of Hemiptera are usuall due to secondary bacterial nfection or personal hypersensitivity

Kwashiorkor Report of Four Cases from Louisiana occurring i Negro hildren is presented by W Medd Hen ng ton, Edward Caroe, Vincent Derbes and Barrett Kennedy[2] (New Orleans) Kwashiorkor is a protein-deficiency disease first observed in equatorial Africa and since reported in various parts f Asia, Europe and Central and South Africa. The p esent cases are believed to be the first reported in the U ited States.

The fi st patient, aged 11 had continuous om ting and diarrhea w th passage f semiformed stool containing undigested food, ascariasis profound manition, generalized edema a sociated with hypoproteinemia and anemia, cl n cal

(2) A.M.A. Arch Dermat. 78:157-170, August, 1958

should be saved After surgery the patient should never be without elastic support during the day especially if sizable skin grafts have been used

The author recognizes two indications for sympathectomy or repeated sympathetic blocks in patients with postphlebitic syndrome. When the leg is cold and clammy and shows diffuse vascular pain repeated blocks or sympathectomy are useful When the postphlebitic leg shows reflex hyperhidrosis and recurrent weeping eczema, sympathectomy dries the skin and helps healing of the resistant eczema

Clinicopathologic Study of Skin in Mongolism. David W Kersting and Ionel F Rapaport[9] demonstrated localized chronic hyperkeratotic lichenifications on the skin of 74.6% of 232 mongoloid patients The lesions were clinically and pathologically consistent with lichen simplex chronicus Some lesions showed a superimposed subacute eczematous reaction Signs of excoriation were rare In 90% of the group of mongoloids generalized ichthyosiform xeroderma was present In patients in whom it was not present usually younger mongoloids eczema and lichen simplex had not appeared.

A characteristic feature of the mongoloid syndrome is generalized ichthyosiform xeroderma Its cause is unknown The authors believe that the generalized xerosis provides the abnormal dermal substrate for development of secondary eczema and lichen simplex chronicus

Examination of 204 patients with cerebral palsy showed that 35% had some chronic lichenified eczema of the same type found in the mongoloid a significantly lower incidence

Insect Bite by Arilus Cristatus North American Reduviid. Francis D Smith Norman G Miller S J Carnazzo and William B Eaton[1] (Omaha) report a case The patient was a boy aged 10 months who had a painful but otherwise uncomplicated transient lesion The insect i generally distributed over the southeastern two thirds of the United States and can be identified by a semicircular serrated cre t resembling the edge of a cogwheel on the top f the th rax (Fig 31) It has a three-jointed proboscis or beak which is long and stout and when not in u e i bent ventrally un ler the head

(9) A.M A. Arch. Derm 77 319 323 March, 1 8

(1) Ibid pp. 324 339.

lermatoses of kwashiorko are pa nless pos ibly in part be-ca se f the apathy of the patients.

Hypochrom trichia is characteristic Minimal changes in colo n rol the periphery and produce a halo effect. Coloration may be light brown, reddish, golden, gray or wh te Relapse may be reflected by the presence of striped hair

Sk mmed milk has been most frequently used in the treatment of kwashiorkor It is a convenient source of protein of h gh biologic value. Small, frequent meal should be gi en w th a high proportion of m'lk and, in the beginning ex trem l l ttle fat. If the patient requires treatment urgently th mplest way t adm nister the necessary protein is by epeated tran fusions of packed ed blood cells

* [\ is pointed out her by Henlington and his co-workers, malnutrition orldwide problem and therefore Kwashiorkor may be expected to xcur in many part of the world. Fortunately malnutrition is uncommon in the United States, hich must account in part for the fact that this is the first report of the disease from this country —Eds]

Cutaneous Lesions of Rheumatic Fever Clinical Study in Young Adults. During 18 month Orlando Canizares (New Y rk) bserved 233 cases of rheumatic fever in an army air f con alescent center A special effort was made to detect dermatoses pos bly related to rheumatic fever Those whi h ould not be elated were ex luded from the study

C t neou changes du t the primary disease were obse ed 4 patient (10.3%) These included urticaria, purpura erythema nodosum, subcutaneou nodules and ery th ma m ltif rme There were 4 cases of urticaria. In all case th ppearan e f wheal wa related to exacerbations f the d sease and t invol ement of new joints. Sedimenta t on rate w s high A acute symptoms subsided urticaria l sappea ed Cases of urticaria easily traced to other causes uct f od were excluded.

l ur case f erythema nodosum were f und with typical lesion the terior urfaces of the legs In each case the nod t m ppeared at the height of the rticula nvolvem t when the sedimentation rate was ele ated and the P R t rval long There w r no el pses

l ythem c eruption local zed t the legs and ankles oc rred 5 patients. These lesion ppeared gradually usu ll t the height of articular in ol ement, although n 2 pa

) N Y Arch Dermat 762 707 December

enlargement of the liver a reddish tinge of the ends of the hair apathy and mental retardation and scaly follicular skin changes over the chest The fourth patient, aged 20 month had vomiting ascariasis los of weight generalized edema, weakness and pronounced mental apathy Her hair did not show a reddish tinge but was lighter sparser and drier than usual Negroid hair The second and third patients aged 4 and 3 sisters of the first pre ented typical manifestation of kwashiorkor but in a milder (*forme fruste*) form. All 4 children improved on a better dietary regimen

Diagnosis of kwashiorkor is made on the basis of the fol lowing manifestations (1) retardation of growth (2) dy pigmentation of hair and skin (3) edema usually associated with hypoalbuminuria (4) pathologic changes in the liver including fatty infiltration fibrosis and necrosis alone or in combination (5) nutritional dermatose which may be absent or present in a variety of patterns, (6) ga trointe tinal disorders which may include anorexia digestive upset diar rhea and mild steatorrhea (7) peevishness and mental apathy and (8) a high mortality if the condition is untreated or if it is incorrectly treated *Differential diagnosis* includes pellagra cirrhosis of the liver and carcinoma of the liver

In mild ca e there may be no definite dermatologic changes. In advanced ca e there may be evere dy pigmen tation varying from bronze t reddi h In white kinned children the fir t change i erythema which blanche on pres ure Thi i rapidly ucceeded by mall purple patches which do not blanch Later the darken and have a waxy feel and sharp raised edges (enamel paint areas) These patches are scattered o er the body but are most numerous over the leg thigh buttock abd men scapular region arms and forearm Within 2 3 day th y hange from their original florid color to dark brown re ldi h brown r black They become dry hard caly and h tin tly rai ed

While new area f enamel paint f rmat e l vel p at the edge of the original le i n the central pl que enlarge Within a week regardle of treatm nt le quamati n oc curs The pale thin epidermi whi h i e p e l ma ulcerate if it does not the expo ed area feel m th and dly In time there is repigmentation of the lepign nted area f th n skin in which overlying enamel p t have been he l The

dermatoses f kwashiorkor are painles pos ibly in part because of the apathy of the patients.

Hypochromotrichia is characteristic Minimal changes in color i volv the periphery and produce a halo effect Coloration may be light brown, reddish, golden gray or white R lapse may be reflected by the presence of striped hair

Skimmed milk ha been most frequently used in the treatment of kwashiorkor It is a convenient source of protein of high biologic alue Small frequent meals should be given with a high proportion of milk and, in the beginning extremely little fat. If the patient requires treatment urgently the simplest way to administer th necessary protein is by repeated transfusions of packed red blood cells

[\ is pointed out here by Henington and his co-workers, malnutrition is orldwide problem and therefore kwashiorkor may be expected to occur in many parts of the world Fortunately malnutrition is uncommon in the United States, which must account in part for the fact that this is the first report of the disease from this country —Eds]

Cutaneous Lesions of Rheumatic Fever Clinical Study in Young Adults. During 18 month Orlando Canizares (New Yo k) bserved 233 cases of rheumatic fever n an army a r f m con alescent center A special effort was made to detect dermatoses possibly related to rheumatic fe er Those which could not be related were excluded from the study

C taneou changes due to the primary disease were observed in 24 patient (10.3%) These included urticaria, purpura, erythema nodosum, subcutaneous nodules and erythema multiforme There were 4 cases of urt caria. In all cases the appearance of wheal w related to exacerbations f the disease a d to involvement of new jo nts Sedimenta t on rat was high. As acut symptoms subsided, urt caria d sappeared. Cases of urticaria easily traced to other causes uch f od wer excluded.

F ou ses f erythema nodosum were fou d with typical les on the anterior urfa es f the legs. In ea h case the and t m ppea ed at the height of the articular in olvement when the sed mentatio rate was levated nd th P R t n l long There were no elapses

P rp ric eruption localized t th legs and ankles oc rred n 5 patients. These lesio s appeared gradually usu ally t the height of articular n ol ement lthough n 2 pa

tients they developed early in the disease. The course of the eruption varied from 3 to 5 weeks.

Three patients had subcutaneous nodules near affected joints After several weeks or even months, the nodules slowly disappeared leaving no sequelae.

Four patients had papular erythema multiforme. The lesions were split pea size dull red papules on the back of hands and feet and the extensor aspects of arms and legs. They appeared gradually were asymptomatic and lasted 3-4 weeks Annular erythema developed in 4 other patients.

The terminology of the ringed eruption of rheumatic fever in the literature is confusing To confine the term erythema annulare rheumaticum to the flat type and erythema marginatum rheumaticum to the elevated type is impractical since many transitions can be found between the two types. The term erythema multiforme rheumaticum (annular type) is suggested for this group

Granuloma Faciale Report on Case is presented by Madela H Foss[4] (Rikshosp Oslo)

Woman 38, was first seen in 1947 with a walnut sized, bluish, slightly elevated firm elastic tumor at the right mandibular angle (Fig 32) Similar but smaller lesions were located behind the left ear on the right ear on the upper lip and in the scapular region. Histologic examination revealed acute inflammation of the skin, but



Fig 32.—Tumor at right mandibular angle in 1947 (Courtesy of Foss, M H Acta Dermat.-venereol. 37 471-482 1957)

(4) Acta dermat.-venereol. 37:471-482, 1957

because of the clinical picture, suggestive of malignancy the patient was treated with radium. This was followed by chronic ulceration of the lesion t the angle of the mandible, reduction in size of the lesion on the right ear and disappearance of the other smaller lesions.

Healing of the ulcer due to radiotherapy of the lesion at the angle of the mandible occurred slowly and was followed by formation of a scar surrounded by an elevated, bluish marginal zone which gradually increased in size during the next 10 years. During thi period the patient had constant pain in this area.

In 1957 the lesion was 8×4 cm., bluish to brownish red, firmly elastic, well defined and involved the cheek in front of the right ear I the center there were cicatricial changes at the site of the previous radium application. Smaller bluish nodules were present on the right side of the nose and at the opening of the right auditory canal

Biopsy of the marginal zone of the large plaque showed nodes of granulomatous tissue, rich in cells, situated deep in the corium. The infiltrate consisted f many neutrophilic granulocytes and lymphocytes, some plasma cells and eosinophilic granulocytes and slightly swollen, pallid histiocytes. Microscopic diagnosis was granuloma (probably granuloma faciale)

(ran loma faciale is usually asymptomatic, and the pain in th present case is believed to have resulted from radioderm tis rather than the granuloma tself Surgical moval f well-defin ed plaques of granuloma faciale s sometimes suc essf l but in this case surgical treatment does not seem ind cated, because of the si e of the lesion and the probability f poor healing in the treated area.

Generalized Micropapular Dermatosis of Reticulofibrocyt ic Structure, Accompanied by Specific Changes in Stroma (New Type of Cutaneous Reticulosis?) This report by St. Gh Nicolau and L. Balus (Bucharest) was stimulated by a recently publ shed description of a milar case (Th ers *et al.*, 1957) in which there was sclerodermiform infiltration of the hand cutaneous infiltration of the face and confluent papu la lesions of arms and thorax. Histologically there was sig ificant proliferation, w th degeneration of elastic fibers compa ed by fibroblastic proliferati n, justifying classification generalized diffuse fib oelast ldosis. The authors beli that these 2 cases represent a new erupti e entity but the ha used different term nology because their interpretatio of the condition d ffers from that of Thiers.

Woman, 55 had generalized dermatosis which had begun with a reddish swelling between the eyebrows and about 8 months later had extended to other parts of the face the neck, sternoclavicular regions

(5) Ann dermat et syph 86 144- 56, Mar Apr 1958

and extremities (Fig 33) At the beginning lesions consisted of isolated micropapules, and they coalesced later to become plaques of diffuse infiltration of a type almost sclerodermiform. These lesions were of variable size As the eruption developed, the skin began to thicken and become indurated. Appearance of the skin disorder had coincided with appearance of the menopause. The lesions of the face gave a peculiar appearance, as if the patient were frowning There was no impairment of general health

Histologically the micropapular element consisted of a proliferation of reticular cells with an obvious tendency to become fibrocytic, paralleling a sclerohyaline reaction of connective stroma.

In considering the histologic characteristics of the infiltrate which marks the condition as a systemic disease the authors suggest that it may be a particular type of benign cutaneous reticulosis It is difficult to classify this case among known types of cutaneous reticulosis in which presumably the initial cytologic type persists throughout the duration of the disease It is suggested that besides the classic orthoplastic reticuloses, there may be a metaplastic type characterized by transformation of reticular cells into fibrocytes capable of causing a sclerohyaline degeneration of the connective tissue stroma Clinically this new type of reticulosis is differentiated from other types by the monomorphism of the eruption with micropapules which tend to coalesce to become a diffuse infiltration in the midst of which the papules are difficult to distinguish except at the edge of the plaque in areas recently invaded by the eruption



Fig 33 — Upper end of plaque involving right upper arm, showing granite appearance due to micropapules in mass. (Inset: Micropapules may be better seen as isolated elements in deltoid region recently invaded. At left, small area of skin not involved due to vaccinal scar in eruptive plaque. (Courtesy of Nicolau, S G and Balus, L. Ann. dermat et syph 85 146-156, Mar-Apr 1958.)

Miescher's Granulomatous Cheilitis with Multiple Cutaneous Manifestations Suggesting Lupus Erythematosus is reported by X Vilanova J Pinol Aguade and C Carlenal[6] (Barcelona)

(6) Ann dermat. et syph. 85 278-289 May-June 1958

Boy, 14, retarded physically and mentally was examined on Oct. 18, 1946. Four years previously red spots had appeared on the back of the hands and then on the fingers. Almost simultaneously a deep fissure developed in the mucous portion of the upper lip, which persisted, despite some improvement during the summer months. Insidiously and without acute inflammation or change in the general health, the whole upper lip increased slowly in size and numerous crevices appeared on its mucous surface.

On examination, the lip was double normal size. The skin was slightly purplish and palpation showed total, elastic infiltration which extended to the nasal roots. The red edge of the lip showed deep me-



Fig. 34. Granulomatous cheilitis. (Courtesy of Villanova, X. et al. Ann. dermat. et syph. 85 278-309 May-June, 1958.)

than crevice which extended to the gums. There were also other smaller fissures (Fig. 34) covered by scabs of bleeding ulcerations. Labial mucosa and gums, corresponding to the region of both canines and the 4 upper incisors, were swollen and presented a granular surface covered partly by diphtheroid pseudomembrane. The tongue ... furrowed. Nasal mucosa was covered by scabs and purulent exudate which extended onto the nostril.

Lesions on the hands and fingers were purplish erythematous spots, of slightly ragged appearance (atrophic) covered by very fine and adherent desquamation. Submaxillary and right axillary lymph glands were swollen and hard.

Careful general neurologic, endocrinologic and radiologic examinations revealed no other abnormalities. Biopsies were made of the hypertrophic lip, nasal mucosa, cutaneous lesions of hands and fingers, as well as a study of tissue response to inoculation with Kveim's liquid by scarification and by intradermal injection.

A squamous erythematous lesion of the finger showed hyperkeratosis, accented in follicles and sweat gland pores. Epidermal atrophy was present, with only 2-4 layers of epidermal cells. Interpapillary buds were extremely thin. The dermis showed a diffuse infiltrate limited to the papillary body and formed only by lymphocytes and histiocytes. At various points this infiltrate surrounded the basal layer and destroyed it. The basal layer had lost its normal appearance and in its place were epineural cells which here and there showed some necrosis. There was mononuclear exocytosis at some points, capillary vasodilatation with increase in size and number of endothelial cells and thinning of connective tissue and disappearance of elastic tissue in the area of the infiltrate edema was mild. In the upper lip a large compressed infiltrate occupied all the dermis, composed of histiocytes, lymphocytes and some plasma cells, with no polymorphonuclear cells. In this infiltrate there were masses of epithelioid cells centered by multinuclear cells. Connective tissue fibers and the elastic network were entirely dissolved in infiltrated regions. Tuberculoid formations were also found within the infiltrate.

The patient was given streptomycin hydrazide vitamin D_2 and prednisone without benefit. Later with radiotherapy (450 r) edema, induration and ulcers of the lip disappeared almost completely and the primary median fissure was treated surgically with good result. Lesions on the hands improved progressively and, at the last examination appeared merely hypochromic and slightly atrophic. Lesions persisted in the ungual skin folds. A small erythemato-squamous lesion which appeared in the left ear disappeared spontaneously within a short time. Around an old scar on the left side of the forehead, a slightly erythematous, poorly limited area had been noticed for several weeks, with points of atrophy slightly rough to the touch and traversed by fine rare telangiectasias.

Despite a clinical and histologic similarity to lupus erythematosus, the authors do not believe that the lesions represent this condition. They suggest the possibility of an extrafacial localization of a generalized or systemic disease in which granulomatous cheilitis is usually the major manifestation but which could be expressed also by other signs of pluri- oligo- or monosymptomatic type.

Eruptive Collagenosis with Multiple Foci and Metachromasia was observed by *J. Gay Prieto, P. Rodriguez Perez* and *M. Alvarez Cascos*[7] (Univ. Skin Clinic, Madrid).

Man, 44, was hospitalized because of skin eruption. Examination revealed nodules of pinhead to millet size on the upper part of the body, abdomen and thighs. They were yellow and spheroid, especially on the abdomen, and seemed to contain gelatinous material. On the back, thighs and upper arms, the nodules appeared crowded, formed a reddish yellow plaque, were smooth and did not itch. The mucous membranes appeared normal. Blood study showed increased

(7) Hautarzt 9 300-304, July 1958

gamma globulins. Itching disappeared on 250 mg cortisone daily X ray treatment to a small focus on the back failed.

Histologic studies revealed that the nodules consisted of newly formed connecti tissue cells. The collagen fibers were swollen, slightly basophil and difficult to recognize. With silver impregnation the fiber net was well isible Metachromatic staining with toluidine blue and thionine showed red-stained substanc between the colla gen fibers of the nodules. I fresh nodules, the process seemed to be gm w th hromatic collagen hanges. Between the nodules there were tw characteristic changes (1) minimal perivascular infiltration and ( ) ccumulation of numerous mastocytes, giving the appearance f mastocytosis.

The basic hange seemed to be collagen transformation. In upport of this was the slight increase of globulins over album n. For this entity which has not been described yet, the a tho propose the name erupti e collagenosis with multipl m ta hromati foci. The disease also affects the glom ruli, as seen n biopsy specimens. S milar glomerular changes are found in acute lupus rythematosus.

Familial Mediterranean Fever Harry Heller Ezra Sohar d Libby Sherf[8] (Tel-Hashomer Government Hosp., Tel \ ) describe heredof m lial syndrom occurring in per son f Med terranean tock The disease i haracteri ed by tta k of fe er small brief recurring at rying ntervals d ccompa ied by pain in the abdomen or chest, one or m lt j l jo t a combination of these regions. In many pat t rs ipelas-l ke patches of erythema ppear on the lower trem ties n ually n the ankles or dorsa of the feet, b t occasionally o th calf Most of patients are non-Ashkenaz Jew or Armenia In about 60% of cases the disease ffect mo tha one member of a family Onset is lmost alway the 1 t or 2d decade.

During bdominal cri es pai usually d ffuse nd soon becomes t emel severe Early the bdomen is somewhat dough but later a boardlike hardness frequently develops. I pat ents s bjected to laparotomy during an attack gross pathologic lesion re bsent Signs of improvement usually ppea (1 hours fter onset of an attack. Chest pain is less common than abdom nal pain It is located n th lower thorax, small on on side. It is tabbing in character and n ten fied b deep b eathing Usually decreased breath sounds t the l ng base are the sol physical findings. The attack bsides fter 12-48 hours Most patients with arthralgia

8 A. Arch. Int. Med. 102:50-71, July 1958.

show redness and swelling of the involved joints. Occasionally however no objective signs are present. Even joints totally immobilized during an attack usually regain complete normal form and function immediately after the crisis. Between attacks clinical examination is negative apart from possible splenomegaly. Laboratory examination usually reveal a rapid sedimentation rate spherocytosis increased fibrinogen and in many cases proteinuria.

Recovery has not been reported in familial Mediterranean fever. Attacks may occur for many years, sometimes with remissions lasting several months. Death in all cases has resulted from renal insufficiency. At autopsy extensive amyloidosis is found. Histopathologic investigations during life have revealed meager findings if any which can be regarded as specific.

Nothing certain is known concerning etiology and pathogenesis. No effective treatment exists. ACTH and cortisone will not terminate or prevent attacks. These drugs are believed by some to enhance deposition of amyloid material and their use seems contraindicated in this disease.

The authors found many examples of this disorder in the literature. It has been called by various names the best known of which are probably "benign paroxysmal peritonitis" and "periodic disease." The authors present data on 14 previously unreported cases. The name "chronic recurrent, heredofamilial Mediterranean fever" or in short "familial Mediterranean fever" is suggested.

► [This article on familial Mediterranean fever is included in the Year Book because of the erysipelas-like patches of erythema of the lower extremities which may create confusion with other cutaneous syndromes.

Heller *et al.* believe that many cases of familial Mediterranean fever have been described under the heading of "periodic disease" but they feel that familial Mediterranean fever is not identical with the periodic disease described by Reimann (*J.A.M.A.* 136:239, Jan. 24, 1948) which is also associated with cutaneous manifestations including angioneurotic edema and purpura.—Eds.]

Parapsoriasis Varioliformis and Its Histology was studied in 5 cases in which 21 biopsies were made by J. Tierard (Gent) and E. P. Van Steenbergen (Utrecht). In this condition along with papulo- and maculosquamous lesions of parapsoriasis, there are purpuric hemorrhagic lesions, papulovesicles or papulopustules and blackened scabs covering small necrotic ulcers. Systematic study of the evolution of the varied lesions

(9) Ann. dermat. et syph. 84:430-446, Nov.-Dec., 1957.

demonstrated successi tages from the squamou papule to the ves cular element o to lo of substance characteri tic of parapsoriasis variolif rmis, which is followed by a 1 atrophic scar

One patient had acute parap-oriasi ariolif rm wh ch lasted 3 months and 4 had a more chronic course which p esented all arieties of the multiform lesions

Case 3.—Indonesian man, 26, had a skin eruption which had begun 3½ months before in the axillae nd popliteal creases and had extended within a few weeks to the trunk and extremities (Fig 35) At the beginning, there was small papule covered with vesicle. When these dried up, there was pronounced itching Examination revealed an exanthema scattered symmetrically on the neck, trunk, arms composed of arious lesions (1) rounded lenticula red-brown papules with violet center ( ) macules with a central scab (3) larger lesions 4-6 mm in diameter red and papular some with fluid elevation at the center resembling a blister and others with slightly depressed necrotic scab (4) numerous pigmented spots, 3-4 mm., with central atrophy

The changes produced by the varioliform proces n th initial histologic lesion of parapsoriasis guttata are deuced principally in increased abundance of intraep d rmal edema with a tendency to ca ity formation the epithelial cellula hanges leading to necrobios (F g 36) presence f ascular lesion and diapedesis of numerou blood cell \ edema increases and the lesions become more complex, w th lacunae more numerous and voluminous, fusion of these ca ities gives rise to the vesicles containing epithelial ll m rious tages of degeneration and cellular a d nu clea debris f lymphocytes red cells and some polymorpho u lea cell and fibrin filaments. These changes occur along w th b ou lesion of epidermal cells edema homogeniza tion of protopla m w th disappearance of reticular struc tu e cavitary change and polymorphous degeneration of nu lei Th final res lt death of the cell which may be trans f rmed nto hyalm or be completely lysed In th extrem tage the entire epidermis is necrosed with the papillary derm and thus gives rise to formation of a layered scab on ting of debri of all lved cellular element \ ascu l lesion begin with congestion progress to nfiltration of th wall, and, in necrotic stages its destruction. These vascula hanges explai th presence of red blood cells in su perficial a d middle dermal layers which may be seen even

50μ

F[ig.] 35 (top) Parapsoria[sis] … [varioli]form …

Fig. 36 (bottom) Section of epidermis composed of … superimposed l[ayers]. Upper (dark) result of necrobiosis … in process of … Immediately below light band is regenerated epidermis … … inflammatory process of parapsoriasis … evident … presence of small … and soft dermoepidermal border. Lower dark band represents dermal collagen.

(Courtesy of Pierard, J. and Van Steenbergen, P. P.: Ann. derm. et syph. 84:630-646, Nov.-Dec. 1937.)

in less differentiated lesions. When a histologic section resembles that of parapsoriasis guttata with pronounced cellular changes in the epidermis and red blood cells in the dermis, parapsoriasis varioliformis should be suspected. The classic lesions of parapsoriasis guttata pass almost imperceptibly into the more varied and eventually completely different lesions of parapsoriasis varioliformis.

Unusual Case of Dermatitis Factitia is reported by Abraham Zelony[1] (Patchogue, N. Y.).

Woman, 59 and obese psychiatric patient who refused to answer questions, was referred for dermatologic consultation with a tenta-



Fig. 37.—Lesions measuring 2 mm. on abdomen. (Courtesy of Zelony: A.M.A. Arch. Dermat. 78:398-399, September, 1958.)

tive diagnosis of petechiae of undetermined origin. There were L. 15 round, violaceous, slightly depressed, atrophic lesions on the abdomen (Fig. 37). Numerous scattered, small, firm, intradermal and subdermal nodules were palpable in the skin of the abdomen. Many of the nodules were not associated with the visible lesions. Because the lesions were not truly petechial and did not fit a pattern associated with a specific dermatitis, a diagnosis of dermatitis factitia was entertained.

When attempting to biopsy one of the lesions, the cutting instrument touched a rigid object with a metallic click. A small hemostat was then used to remove an ordinary sewing needle. An x-ray (Fig. 38) confirmed the impression that the other lesions were also caused by similar foreign bodies. Apparently most of the needles were in-

[1] A.M.A. Arch. Dermat. 78:398-399, September, 1958.



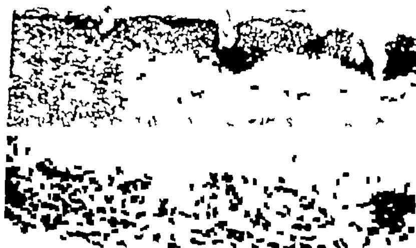


Fig 35 (top) Parapsoriasis [illegible] formis

Fig 36 (bottom) Section of epidermis composed of two superimposed layers. Upper (dark) result of necrobiosis, in process of elimination. Immediately below, light band is regenerated epidermis attacked [illegible] by inflammatory process of parapsoriasis varioliformis evident, intense exocytosis, presence of small cavities and soft dermoepidermal border. Lower dark band represents dermal collagen.

(Courtesy of Pierard, J. and [illegible] Steenl [illegible], F. P. Ann dermat et syph 84 630-646 Nov Dec 1957)

left hand. From time to time small pieces of white chalky material discharged through the skin covering the masses. Seven years ago she noticed the gradual ppearance of a similar but larger mass just be neath the skin of the lateral surface of the middle third of the left leg. Shortly after an attack of superficial phlebitis of the left leg 2 years ago, small piece of hard white material discharged through the skin of the leg. Healing as prompt, but second piece of chalk discharged 22 months later. This time an ulcer formed at the sit of



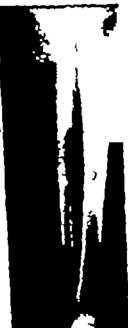


Fig. 39. Fig. 40.
(Courtesy of Boyd, B. Brit. J. Dermat., 70 107 109 March, 1958.)

discharge. Examination revealed gross internal saphenous veins with edema of the lower tw thirds of the left leg. On the lateral aspect there as a reddish area containing 3 small sinuses (Fig. 39). Beneath each sinus a hard plaque could be felt and on looking down a sinus, hite chalky material could be seen beneath the skin. This radiopaque (Fig. 40). The volar surface of 3 fingers of the left hand contained several small radiopaque deposits similar to that in the leg. Juxtafemoral ligation of the left internal saphenous vein was performed, and the calcareous concretion was removed from the ulcer. Elastic adhesive ambulatory compression was used, and the ulcer healed in 4 weeks.

(W ha had under our care woman with chronic dermatitis of the lower extremities and an indolent ulcer on one shin which had failed to



Fig. 38.—X-ray of abdominal region showing presence of numerous foreign bodies. (Courtesy of Zelnoy, A.: A.M.A. Arch. Dermat. 78:398-399, September, 1958.)

serted with no visible skin changes resulting. In a few instances the chronic trauma of the skin by a needle not as yet completely walled off by fibrous tissue resulted in a local red area of atrophy. The atrophic skin was pigmented from hemosiderin which appeared after injury to the capillaries.

► [This is one of the very unusual cases of factitious dermatitis which are reported from time to time. No such thing here as looking for *one* needle in the haystack!—Eds.]

Calcinosis Circumscripta Presenting as Varicose Ulceration. Calcinosis circumscripta is a rare condition occurring mainly in women of middle or advancing years who show scattered calcareous radiopaque concretions in the subcutaneous tissues about the joints of the upper and lower extremities and pelvis. The cause is unknown. Stanley Rivlin[3] (London) presents a case which appeared as varicose ulceration.

Woman, 63, had had varicose veins for 20 years. Thirteen years ago she became aware of small, hard lumps in the pads of 3 fingers on the

(3) Brit. J. Dermat. 8:107-109, March, 1958.

ga marked eaction for phosphates with Kossa s stain and appeared to be calcification.

C se ——Miner 21 had groups of small white papules arranged in line on the left elbow He had probably braded the elbow be fore onset of the eruption, but he could not remember a particular injury The histologic picture was not identical with that seen in Case 1 since there was a break in the epidermis, and the gap was filled with metachromatic structureless material which did not stain completely with Kossa s reagent.

Both patients worked in a section of the mine where roof w ter containing 3.5% calcium chloride dripped on them. This water appeared to be the cause of the cutaneous lesions. Similar lesions were produced experimentally on the skin of one of the authors by applying 3 5% calcium chloride solution to a scarified area on the forearm (Fig 41) for 72 hours. Th experimental lesions cleared in 6 weeks the miners recovered n 4 months.

► [An interesting series of events The authors speculate on the possibility of such mechanism playing a role in the formation of renal calculi. —Eds.]

White Lesions of Vulva Discussion of Lichenification (Lichen Simplex Chronicus) Leukoplakia, Bowen s Disease, "Kraurosis Vulvae, Lichen Sclerosis et Atrophicus, and Senile and Essential Atrophies of Vulva is presented by Arthur B Hyman and Henry C. Falk (Beth Israel Hosp New York) Lichen simplex chron cus leads to a thickening of the skin with increased skin markings, better appreciated the gro n and on the pubis and thighs than on the labia majora. The outlines are usually less well defined than the plaques of leukoplakia, and the color is brownish or ery thematous rather than dead white. Leukoplakia is essentiall disease of the mucosa or mucocutaneous tissue. The skin ar und plaques of leukoplakia may show lichenification due t long-conti ued scratching Erosions, ulcers or keratoses leukoplakia are warning signals of the possible intervention f malignancy but erosions in lichen simplex chronicus, resulting from scratching do not indicate possible card nomatous change

The rough, erracous, outstandingly hyperkeratotic lesion found n most cases of Bowen s disease of the vulva (and in Paget s disease) should make t easy to recognize that more than just lichenification is present. Bowen s disease is particularly a disease which afflicts older adults, and

( ) Obst & Gynec. 12 407 13, October 1958.

heal under many forms of therapy It was not until calcareous deposits at the base of the ulcer were dissected out under local anesthesia that the ulcer eventually healed. These deposits had been shown on x-ray to be linear and associated with nonfunctioning vessels in the area, they were diagnosed as "calcified phleboliths" and calcifications of the veins —Eds]

Traumatic Calcinosis of Skin. I B Sneddon and R. McL. Archibald[3] report 2 cases.

CASE 1—Coal miner 29 had an eruption on the back which appeared 3 weeks after the back was abraded while he was working in

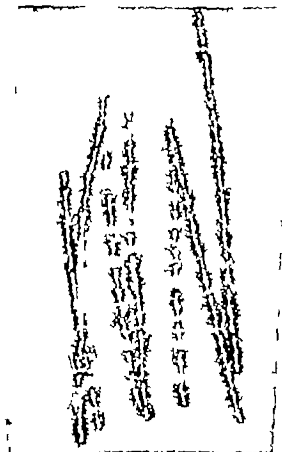


FIG. 41—Experimental lesion produced by calcium chloride solution (Courtesy of Sneddon, I. B., and Archibald, R. M L Brit J Dermat 70 211 214 June, 1958)

the mine. The eruption consisted of firm white papules, 2 3 mm. in diameter some in ring formation and others linear Most were surrounded *by an erythematous* halo. They occurred at the exact sites where the skin had been abraded. Histologic examination showed an intact and normal epidermis. In the upper derm s was a zone which

(3) Brit. J Dermat. 70:211 214 June, 1958.

enification. Gren rays and thorium X are safer Antipruritic applications are useful for symptomatic relief in leukoplakia. Sometimes spontaneous improvement occurs. Vulvectomy should be performed only if there is ev dence of malignancy or mpending malignancy It is the recommended operation for Bowen s and Paget s diseases. Lichen sclerosis et atrophicus shows symptomatic relief with antipruritic agents, and a trial with chloroqu ne orally is worthwhile. Essential tightening of the introitus may be helped by dilators. Estrogens by mouth or locally are not beneficial in any of these vulval diseases.

► [T the conditions listed here which might produce whitish lesions of the vulva one could add lichen planus and moniliasis W agree with the authors that "kraurosis vulvae" has become such an ill-defined and hazy concept that it might be best if the term was abandoned. Dermatologists hav always been alert to the various conditions which are seen on the vulva and have differentiated between those which are "precancerous and those which hav no malignant potential. Unfortunately others on occa sion have failed to make these differentiations and have done vulvectomies in cases of harmless vulvar dermatoses. Hyman and Falk article should be helpful in remedying this situation —Eds.]

Steatocystoma Multiplex with Embryonal Hair Formation Case Presentation and Consideration of Pathogenesis. Miguel A Contreras (Ciudad Trujillo Dominican Republic) and M urice J Costello (New York) report 3 cases of steatocystoma multiplex in wh ch multiple embryonal hairs grouped in brushl ke arrangement were found in typical cy ts. The hairs were similar to those found in trichostasis spinulosa, which the authors bel eve is a co gen tal malformation probably related to steatocystoma multiplex.

W th regard to the pathogenesis, the question arises whether the cysts of steatocystoma multiplex are retention cysts or cysts of new formation belonging to the atheromas or a ev d cond tion. Opinions vary The finding of multiple hairs in the cysts seems to favo the atheromatous nature.

Against the theory of etention cysts are the facts that the cysts are congenital (some patients are born with them) and familial. They are nherited according to mendelian law and often ar ccompa ed by other malformations in the pa tient o their families. They are rare or absent n patients with severe cystic acne The presence of fully developed comedones and acne vulgaris n patients with steatocystoma is also rare The cy ts are symmetrically distributed. It is dif ficult t demonstrate the occluded sebaceous duct, which in

(1) A.M.A. Arch. Dermat. 76 720 725, December 957

it may involve the skin as well as the mucocutaneous tissue

Lichen sclerosis et atrophicus of the vulva involves skin and mucocutaneous tissue. The size of the labial adnexa and introitus may be normal or contracted. The tissue covering them and the vulva as a whole is thinned, the periphery of the diseased areas is usually well defined and outlying flat topped atrophic papules may be seen. The cigaret-paper wrinkling of the surface of affected sites is characteristic. Itching is prominent so lichenification is apt to be an associated feature. Classic lesions of lichen sclerosis et atrophicus may be found on other areas of the skin.

In purely senile changes of the vulva the introitus is not narrowed. The labia shrink and are absorbed. Unless complicated by other conditions there is no pruritus or other symptoms.

Narrowing and tightening of the introitus usually with diminution or disappearance of the labia but without thinning of the skin are a rare combination that may be found at all adult ages. Patients usually come for consultation because of dyspareunia or difficulty and pain on insertion of a pessary. Very little is known about this group. These cases are the only ones for which the term kraurosis vulvae (essential narrowing of the introitus) is justifiable. It is possible that they belong to the group of scleroderma.

With a good clinical history and clear indication of the biopsy site, leukoplakia and lichenification may be distinguished microscopically, but without these histologic diagnosis is largely guesswork. The most important histologic finding in Bowen's disease is the great variety of cell and nucleus types found within the epidermis. The microscopic picture in lichen sclerosis is characteristic. Senile vulval changes seldom show striking features. Atrophy is more definitely recognizable clinically than histologically. The authors believe that cases reported as kraurosis vulvae with a histologic picture of lichen sclerosis et atrophicus are actually examples of the latter disease. They consider it untenable to distinguish between kraurosis and lichen sclero[illegible] the basis of changes in the vessels of the deep cutis. In any of the above conditions when radiation has been used it may be impossible to unravel the histologic effects of radiation from the microscopic features of the disease proper.

The authors advise against repeated x irradiation in lich

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(1) A.M.A. Arch. Dermat. 76:720 723 December 1957

most instances is not present The cysts contain nonoxidized fat in contrast with the oxidized fat in retention cysts. They sometimes occur on the palms and soles where the pilosebaceous glands are absent. On the basis of the findings in their cases the authors favor the hypothesis that the cysts are of new formation on a nevoid basis

Fox Fordyce Disease with Hidradenitis Suppurativa. Pore closure is a feature of both Fox Fordyce disease and hidradenitis suppurativa. It might be logical to suspect that the two diseases would often be found together but Rachel Ford Spiller and John M Knox[6] (Baylor Univ) found only 1 report of hidradenitis suppurativa as a complication of Fox Fordyce disease in the English literature. They present 3 cases in which the disorders occurred simultaneously

Negro woman, 33 had deep painful nodular lesions in the axillae. Many small, flat-topped papular lesions were present in the axillae, about the nipples and in the vulvar region. These lesions were extremely pruritic and had been present 10-12 years. The hidradenitis suppurativa responded promptly to therapy The pruritus associated with Fox Fordyce disease was relieved by oral Terramycin® but various forms of treatment, including vitamin A, antihistamines, Gantrisin® and topical hydrocortisone had no objective effect on the papular lesions.

Pathologic examination showed the stratum corneum to be irregular with alternate areas of normal thickness and hyperkeratosis. In some areas there was pore closure with keratinous plugs in the ducts. Underlying the plugs, the ducts were dilated and surrounded by intra and intercellular edema The rete ridges were elongated and broadened. The superficial dermis was normal. Deeper there were many foci of inflammatory cells, primarily about eccrine and apocrine glands. A large abscess was present in the deep dermis.

The superficial histopathologic changes in this case were those of Fox Fordyce disease and manifested clearly the classic sweat retention vesicle near the pore outlet The large abscess in the dermis was non pecific but characteristic of those found in hidradenitis suppurativa. The anatomic location of obstruction or the presence of secondary infection may determine whether Fox Fordyce disease hidradenitis suppurativa, or both develop in a given patient.

Perianal Hidradenitis Suppurativa Clinical and Pathologic Study is presented by Markham J Anderson Jr and Malcolm B. Dockerty[7] (Mayo Clinic and Found.) Of 117 patients with perianal hidradenitis suppurativa 65% were

(6) J. I vest. Dermat. 31 127 135 August, 1958
(7) Dis. Colon & Rectum 1 23-31 Jan.-Feb 1958.

males. The perianal region is in olved in about 1 of every 6 cases and is the only site of lesions in 1 of every 13 cases. Hi dradenitis may also involve the neck, face scalp extremities, shoulders and abdomen.

Anal fistula secondary to hidradenitis is rare. Hidradeni tis n the postsacral area is easily confused with pilonidal disease especially if other parts of the body are not involved. The term perianal hidradenitis is used rather loosely since many patients with disease in the anal region also have involvement of the scrotum, buttocks, proximomedial aspects of the thighs and the inguinal and pub c regions. A line of demarcation usually does not exist between the anal nvolvement and that of other regions

The cause and pathogenesis of hidradenitis suppurativa are not well understood. Study of the 261 sections taken from the surgical specimens in 64 patients disclosed that ec crine glands were present in 59 whereas typical apocrine glands were identifiable in only 7 The apocrine sweat glands apparently are not of great importance in the pathogenes s f this disease their involvement appears to be coincidental The disease seems to have some relation to endocrine activ ty a d t is l'kely that common etiologic factors are present n hidraden tis and acne Other than the presence of apocrine gland local conditions exist that might help explain the t pical distribution of hidradenitis suppurativa. Among these are the frequent apposition of cutaneous surfaces, excessive local moisture, heat and friction, and the difficulty of maintaining cleanliness in the regions frequently involved.

T eatment of hidradenitis of the perianal region is somewhat discouraging because many patients continue to have ec rrences, e en after careful excision of all acti e sites Until the cause and pathogenesis are better understood, t doubtful that prognosis will improve.

* [The finding that eccrine glands are present in 57 of the 64 cases hich were studied histologically seems to contradict accepted concepts of the role of apocrine glands in hidradenitis suppurativa It is difficult to follow the reasoning of the authors when on one hand they say that apocrine glands apparently are not of great importance in the pathogenesis of the disease (hidradenitis suppurativa) and on the other they suspect that hidradenitis and acne has common etiologic factors, such as endocrine effects Actually such concept would relate the sebaceous and apocrine glands, as it is ell known that the pilosebaceous unit (and not the sweat glands) which is the shock tissue for acne is definitely influenced by certain hormonal changes and that the apocrine glands are also

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(6) J Invest. Dermat. 31 127 133, August 1958.
(7) Dis. Colon & Rectum 1:23-31, Jan. Feb 1958.

Unusual Manifestations in Case of Relapsing Nodular Febrile Panniculitis (Weber-Christian Disease) are reported by Leonard M Goldberg and Leonard W Ritzmann (VA Hosp., Portland Ore.) The patient, a man, 39 had manifestations considered diagnostic of Weber-Christian disease—a chronic febrile illness with recurrent subcutaneous inflammatory nodules that histologically showed the classic picture of fat necrosis, and in healing left atrophy pitting and hyperpigmentation of the skin. In addition several aspects of the disease were considered unusual. Every lesion that appeared followed trauma. In some instances the trauma was relatively insignificant. One cutaneous lesion appeared in an area wher the patient had lain on a hard object an ther occurred from a blow on the leg with a reflex hammer The lesions often underwen flammatory process of considered to be unassc ond patient and the patients of several other authors showed suppurative inflammation.

Another unusual feature was extensi e bone involvement. Serial x rays showed the evolution of a typical protrusio acetabuli after a fall 9 years ago It is assumed that the trauma of the fall produced inflammatory necrosis in the ynovial fat of the acetabulum. This severe inflammatory condition then destroyed the acetabular floor On another occasion the patient twisted the right knee. The knee became hot, red and swollen, and aspirations yielded a greenish gray terile pus On other occasions minor trauma resulted in welling of both knees and right nkle. Early radiographs of the right knee showed demineralization of the distal end of the femur and proximal tibia. Serial films showed a return of calcium, but in heavy coarse, rregular striations differing f om the recalcification after demineralization of bone from disuse The coarse irregular trabeculations could have resulted from recalcification of areas of bone underlyi inflammatory tion also occu yncopal episc ause. The ECG abnormal ties wer more acut than would be expected f the myo dial infarction had precipitated the syncopal attack 5 days previously

(1) Am. J Med. 25 780-795 November 1958

influences by these changes. To our knowledge the eccrine glands play no primary role in the pathogenesis of either of the diseases.—Eds.]

Spontaneous Chronically Relapsing Panniculitis was observed in 2 men by A. Faninger and M. Isvaneski[8] (Zrenjanin, Yugoslavia). *The disease lasted for 10 and 6 years* respectively. In both patients the nodes developed continuously during the entire year. In 1 patient the intensity of the disease increased in spring accompanied by general malaise.



Fig. 42.—Boat-shaped retraction of closed and ulcerated nodes of left leg. (Courtesy of Faninger, A., and Isvaneski, M.: Hautarzt 9:372-374, August, 1958.)

Remissions lasted 1-2 months. The nodes evolved in about 20 days. The end of their regression was characterized by a boat-shaped retraction from the skin surface (Fig. 42).

The nodes, which ulcerated occasionally, were hazel- to walnut-sized, painless and adhered to the skin. They were localized mostly on the limbs but were seen also on the trunk. Histologic studies revealed *granulomatous infiltrations*. The patients studied showed the symptoms of Pfeifer-Weber-Christian and of Rothmann-Makai diseases.

The authors suggest that the diseases with spontaneous panniculitis be considered as a uniform group and that the forms seen in the patients studied and those described by Rockl and Thies be interpreted as transitory forms between Pfeifer-Weber-Christian and Rothmann-Makai diseases.

(8) Hautarzt 9:372-374, August, 1958.

cally with intracutaneous injection of saliva antigens prepared by the authors.

[The concept of "aphthosis" or Behçet's syndrome has been steadily widening. It now encompasses not only the mucous membrane, ophthalmologic and genital changes originally included, but also other cutaneous and neurologic lesions. The word "aphthosis" actually means a disease consisting of small defects of the mucous membranes. This is hardly a good term for the nodular lesions in the skin and the neurologic alterations. However, for lack of a better one, the term "aphthosis" can be retained, at least until more becomes known about the cause of this disease.

Much more work seems required to ascertain the significance of the 2-3 week reactions in skin tests with saliva antigen. The specificity of this test can only be established by further controlled studies. Another skin test in aphthosis, using a suspension of material from an active lesion, was suggested by Franceschetti and Jadassohn. Here, too, the specificity of the skin test has not yet been firmly established.—Eds.]

Acrokeratoelastoidosis is discussed by Ismael M. Pomposello and Santiago J. Mosto[2] (Buenos Aires) with 4 case reports. Since Castro's original description in 1952 only 4 more cases have been reported. The authors believe, however, that the condition is not uncommon but that it is classified under other less accurate diagnoses. Any diagnostic difficulty with regard to this lesion is due to lack of knowledge concerning it. The three characteristic features are papulokeratotic lesions, distribution on the hands and feet and attenuation and fragmentation of elastic fibers microscopically. Biopsy also shows marked acanthosis, with hyperkeratosis and granulosis. In the papillary dermis, connective tissue fibers are enlarged and discretely homogenized, with dislocation in the deeper layers, forming a network. All cases so far observed have been in women.

Ages of patients in the present series were 42, 27 (2 patients) and 35. Lesions occurred on the external and internal borders of the palms and soles in all. In 1 patient the joints of the fingers and the thenar and hypothenar eminences were also affected. Single papules were 2-4 mm in diameter. They were rounded and assumed a polygonal shape in areas where they united to form small plaques. The papules were slightly elevated, smooth and white, yellowish white or the color of normal skin. Palpation revealed a certain keratotic resistance. Lesions could be observed more clearly with pressure or by stretching the skin between the thumb and index finger. This delimited a plaque of whitish papules. In 1 case single lesions were distributed in a ring like a rosary. In no case were there any subjective symptoms. The dermatosis was

(2) Arch. argent. dermat. 7: 271-277, September, 1957.

The authors suggest that when the patient fell during a fainting episode there may have been sufficient trauma to the pericardial fat to result in inflammatory fat necrosis. The inflammation could have caused a *contiguous angiitis of a coronary vessel traversing the area with a resultant inflammatory occlusion and myocardial infarction.* A mild fever noted during the first few days of hospitalization could have represented *the usual febrile reaction to the patient's panniculitis* rather than myocardial necrosis.

Nodular Aphthosis, Aphthose en Plaques and Pfeifer Weber Christian Panniculitis Experimental Reproduction of Nodular Lesions in Aphthosis. X Vilanova and J Pinol Aguadé[1] (Univ of Barcelona) studied 6 patients, 4 men and 2 women aged 24-64 with nodular vasculitis a syndrome belonging to the disease group of aphthoses. One patient showed symptoms and signs of the Pfeifer Weber Christian syndrome All patients but 1 had the nodules on the lower extremities. In this patient the cutaneous infiltration appeared as a large plaque in the face. This form of recurrent infiltration which leaves a depression in the affected area has not been observed in aphthosis so far

The histology of the nodules was not uniform probably because the biopsies were taken from nodules of different developmental stages The nodules showed besides fibrinoid degeneration a proliferation of the connective tissue cells of the corium The latter was of tremendous extent only in the plaque-shaped facial infiltration observed in 1 patient where the entire corium was acutely inflamed with considerable involvement of polynuclear cells giving the appearance in some areas of early suppuration Generally the fibroblastic and *histiocytic proliferation was not pronounced in the peri* capillary histiolymphocytic infiltrations The arterioles and medium sized veins may be involved and symptoms of pan vasculitis may be present. The capillaries may be dilated and thrombosed. *The subcutaneous tissues react late and form a* lipophagic granuloma These characteristics allow differentiation from erythema nodosum from tuberculous and nontuberculous nodular vasculitis and from the various forms of panniculitis

The nodules could be reproduced clinically and histologi

(1) Hautarzt 9 389-391, September 1958.

was some indication of cavity formation in a few sudoriparous glands and the epithelium was flattened.

Large doses of vitamin E orally and 3 applications of carbon di oxide snow at 1-week intervals healed the lesions almost completely leaving pink, slightly atrophic, thin and smooth skin.

The clinical aspects and histologic findings conformed to those of elastosis described by Favre and Racouchot, except for the age factor The atypical young age of this patient and of another sailor with the same condition seen but not treated by the author suggests the hypothesis that the external trau matizing factors, such as climate, heat and sun to which these sea-going persons were exposed must have acted on a kin that was already predisposed to early senescence.

► [An essentially identical clinical picture as that described by Sprecher was reported by Berlin (A.M.A. Arch. Dermat. & Syph. 69:683, 1954) as due to paraffin oil in hair preparations. We have since seen several patients in private practice presenting similar picture, each of whom had used hair dressings containing petrolatum or petroleum oils —Eds.]

Dyskeratosis Ichthyosiformis Congenita Migrans Vari ant of Congenital Ichthyosiform Erythroderma. In 1949 un der the name ichthyosis linearis circumflexa Com J de scribed a clinical picture characterized by slowly extending serpiginou and polycyclic lesions, hyperkeratosis of the flex res and hyperhidrosis of the palms, present from birth. Dan lo V Stevanovic and Radoslav L. Pavic (Univ of Bel grade) found only one other report of this dermatosis in the literature They report another case with features identical w th those previously reported, with the addition of the oc casional development of flaccid bullae

Youth, 20, had red scaly skin at birth and since then the skin had never been completely normal. On the trunk and extremities were many annular and polycycl lesions of various sizes with slightly raised edges (Fig 44) On the forearms and legs there was slight desquamation in addition to these polycyclic lesions. Two flaccid bul lae were noted in the groin. I the axillae and in the popliteal and antecubital flexures the skin was hyperkeratotic and slightly brown. The palms and soles showed hyperhidrosis. The scalp was covered w th greasy scales. Microscopic examination of thigh lesion showed thickening of the epidermis, loose horny scale and parakeratosis. I the papillary layer the vessels were slightly dilated, and there was an infiltrate of l mphocytes and histiocytes, mainly perivascula There mild interstitial edema throughout the dermis.

The a tho believ th condition a variant of ichthyosi f rm erythroderma Both dermatoses are present t birth or soon after a d con picuou ly invol e the flexures Both show

A.M. rch. Dermat. 73:425-429 November 1956

discovered casually because of its localization on the hands.

Cutaneous Nodular Elastosis with Cysts and Comedones. A. Sprecher[3] (Genoa, Italy) reports the results in his study of 1 case.

Man, 24, stoker on board ship, thin but in good general condition, had noticed 6 months before the sudden and painless onset of black, *comedone-like, raised points on the temporozygomatic regions* (Fig. 43) bilaterally and symmetrically. The lesions increased progressively in volume and number and, when squeezed, yielded a whitish, rather dry substance. Between the comedones was a limited number of nodular formations the color of pale healthy skin, millet sized and firm. The skin surrounding and between the lesions appeared healthy although it had the characteristic appearance of skin of sea going persons. Clinical and laboratory tests were normal.



Fig. 43. (Courtesy of Sprecher, A.: Minerva dermat. 33:314-319, August, 1958.)

Histologic examination of skin from the right temporal region showed a *thin, atrophic epidermis* with all the various layers thinner and poorly *differentiated*. The superficial dermis had vast areas of degenerated substance in clusters constituting the common reticular structure of the tissue and interspersed with ones of normal or almost normal, tissue *in which elastic fibers and fibrils were visible*. The deep dermis was more compact with homogeneous fibrinoid degenerations *similar to those of granuloma annulare in some points*. Hyaline or amyloid degeneration and mucopolysaccharides were absent. All the specimens showed numerous isolated cystic formations, some closed, some *communicating with the outside through* follicle, often attached to stumps of pilosebaceous system to which were connected normal, or more often, atrophic sebaceous glands. There

(3) Minerva dermat. 33:314, 19 August, 1958.

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The a thor believe this cond tion is ariant of ichthyosiform erythroderma. Both dermatoses re present at birth or soon fter and conspicuously nvol th flexures. Both show

[4] A M A. Arch Dermat 78 625 629 November 958

pruritus hyperhidrosis of the palms and seborrhea of the scalp The occasional presence of bullae in the authors patient is another feature observed in both syndromes. The histologic changes in the patient reported are compatible with this assumption Hyperkeratosis of the palms and soles often found in ichthyosiform erythroderma has not been found in this syndrome. Because of the striking config



Fig 44—Annular and polycyclic lesions of left shoulder (Courtesy I Stevanovic, D V and Pavic, R. L. A M A Arch Dermat 78 625-629 November 1958.)

uration of the lesions and their progressive extension and the general similarity of the syndrome to ichthyosiform erythroderma the term dyskeratosis ichthyosiformis congenita migrans" is suggested

► [Apparently no fungous examination was done on the serpiginous and polycyclic lesions In at least 1 case of congenital ichthyosiform erythroderma it was possible to explain the polycyclic and serpiginous lesions on the basis of superimposed superficial fungous infection (Arch Dermat & Syph 56 834 1947) Perhaps the same mechanism was operative in the patient of Stevanovic and Pavic—*Ed*]

Isolated Dyskeratosis Follicularis. James H Graham and Elson B Helwig[3] (Armed Forces Inst. of Pathology) stud ed 50 examples of the isolated lesion removed from persons aged *22-67* none of whom had more than 1 lesion. The a er age duration of the lesion was 3½ years Most lesions were about the head and neck. Clinically they were usually con fused with cystic lesions, senile keratosis or basal cell car cinoma.

The lesons were single elevated nodules or cysts with



Fig 1.—Base of lesion of isolated dyskeratosis follicularis, showing basal cell hyperplasia, papillomatosis and lacunae filled with acantholytic and dyskeratotic cells. Lesion sharply demarcated from surrounding corium reduced from 1 L. (Courtesy of Graham, J H and Helwig, E. B A.M.A. Arch Dermat. 77 377 389 April, 1958)

raised borders and somewhat umbilicated or porelike centers. Most were brown, but some were flesh colored, yellow red, black, tan or gray They were firm circumscribed, rough and granula to palpation Dra nage, crusting and bleeding wer common, and local itch ng pa n or a burn ing sensation were the usual symptoms

The pecimens were contributed with variou pathologic diagnoses keratosis f llicularis wa the diagnosis n 10 car cinoma in 15 and in 9 th diagnosi suggested origin from eccri e or pocrine weat glands A diagnosis of isolated D rier d sease was mad n 2 cases.

Examination under low power revealed a sharply circum

3) A.M.A. Arch Dermat 77 377 389 April, 958

scribed cup shaped enlarged follicle extending deep into the underlying corium Usually a keratotic and parakeratotic plug filled the follicle except for a cystic space or lacuna formed suprabasally Usually a single follicle was involved The lesion was fairly sharply bounded by what appeared to be the connective tissue sheath of the follicle.

Higher power showed striking basal cell hyperplasia and resultant papillomatosis Multiple minute prolongations extended into the basal epithelium from the suprabasal lacuna. In some areas the epithelium was arranged in whorls simulating pearls. The lacuna was filled with acantholytic and dyskeratotic cells (corps ronds and grains) (Fig 45) The corps ronds contained an eosinophilic hyalin-like cytoplasm and a large centrally placed basophilic nucleus. Some had also an eosinophilic body in the cytoplasm which suggested an inclusion.

The hypothesis that the lesion is caused by an infectious agent probably viral seems most tenable though proof is lacking Excision is the treatment of choice for the lesion tends to recur after irradiation desiccation and curettage Follow up of 36 patients for an average of 5.3 years yielded no evidence of malignant change nor was there a hereditary background of Darier s disease in any patient On the basis of present knowledge the term isolated dyskeratosis follicularis most aptly describes this entity and is preferable to "isolated Darier s disease and other terms that have been used

Keratosis Follicularis Serpiginosa Lutz (Elastoma Intrapapillare Perforans Verruciforme Miescher) Kai Dammert and Tauno Putkonen[6] (Univ of Helsinki) report a case

Boy 16, had had an eruption on the nape of the neck for 6 years. The eruption did not itch and was below the hairline There were 20-30 discrete papules and a number of confluent papules forming dense circinate ridges or rings. The papules were 2 3 mm. in diameter with redness at the edges and a gray keratotic scale in the center The scale was removed with difficulty leaving a bleeding depression. The skin surrounding the lesion was normal except for an area about 3×3 cm. to the left of the midline This area appeared atrophic and was partially bordered by ridges and papules The hairs were preserved in this area, but the normal skin surface was interrupted by several small low light-colored depressions. Near the peripheral ridges were parallel low fold

During a year the configuration of the eruption changed slowly

(6) Dermatologica 116 143-151 March, 1958

A few new papules appeared and old papules coalesced in places, forming new ridges (Fig. 46) The shape of the old ridges changed and breaches appeared in them as the process subsided in places. The peripheral ridge advanced 2 mm. in 1 year

Development of the lesion was studied by serial sections of the keratopapular ridges and the skin adjoining them on both sides. The first change was an increase of elastic tissue in the upper dermis Then followed a keratopapular tage, characterized by a necrobiotic and necrotic process accompanied by granulomatous and simple chronic inflammatory changes. F brous healing marked the final stage in the process. Most of the excessiv elastic tissue had disappeared, but dense aggregations persisted in some papillae where they formed elevated "elastomas."

The author conclude that the clinically active keratopap-



Fig. 46 Lesions of keratosis follicularis serpiginosa on nape of neck, 1 year after first observation. (Courtesy of Dammert, K and Putkonen, T Dermatologica 43 1, March, 1954)

ular stage tart deep at the tips of the rete pegs. Th exces si e elastic ti n invades the ep dermis caus ng destruction of the n ol ed ti sue and an inflammatory reaction. This iew d ffer s mewhat from p evious concepts. The authors found no f llicular changes and could not demonstrate that the hyperplastic nd hypertrophic elastic tissu was a result f degeneration. Intrapapillary elastomas were seen only in area of fibrous heal ng Outsid the ridge r in the keratopapular lesion no dense papillary aggregations of elastic tissue ere observed, and thu uch aggregations in them selves could scarcely be mportant in the development of the papula flammatory stage of the disease The cause of the increased elastic fiber in this disease s not known. How

ever in at least 6 of 7 reported cases onset of the disease occurred at the prepubertal age between 9 and 12 year and thus hormonal influences may play a part

Are Hyperkeratosis Follicularis in Cutem Penetrans and Elastoma Intrapapillare Perforans Verruciforme Identical? According to Z Zambal[7] (Univ of Zagreb) hyperkeratosis follicularis et parafollicularis in cutem penetrans, elastoma intrapapillare *perforans verruciforme* and *keratosis folliсularis serpiginosa* denote the same disease The clinical characteristics are follicular papulonecrotic lesions which may be isolated *circinate serpiginous or grouped* (*verruciform*) The author's patient a woman 23 showed simultaneously circinate serpiginous and verruciform (Fig 47) lesions Along with the *follicular changes* there were *some nonfollicular* lenticular papules and yellowish maculosquamous lesions.



Fig 47 —Verruciform changes over left knee and dorsally from head of fibula. (Courtesy of Zambal, Z. Hautarzt 9 304 311 July 1958.)

The disease process seems *to be basically follicular* The follicular perforation is probably induced by hair and frag

(7) Hautarzt 9:304 311, July 1958.

ments of hair cuticle Without perforation no histologic di agnos s can be made. Histologically bes des the epidermal changes the e are foreign body granulomas with phagocytic fragments and also mycelium like fibers in the follicle (near the place of perforation) The number of elastic fibers within such follicles s usually small. In addition to the h stologically importa t changes of the elastic and collagen fibers in the ubpapillary layer corresponding to cutis hyperelastica the patient presented all clin cal symptoms of the Ehlers Danlos syndrome.

It is suggested that the described dermatosis develops in patients with cutis foll cularis serpiginosa and that it is essentially a dysembryoplastic disease.

Acrokeratosis Verruciformis, according to Jerónimo López González[4] (Univ of Mendoza) was originally defined by Hopf in 1930 as n entity characterized by hard warts local ed ex lusi ely on the hands and feet and appearing during puberty In 1933 Hopf studied 4 cases in which the warts extended to other skin areas. The lesions appeared early at birth or in the first year of ch ldhood.

Acrokeratosis verruciformis is cons dered a nevoid disease because of it f equent association with various types of nevi. It f m lial, e a genodermatosis due to an anomaly of co fication. It affects both sexes equally The lesions are papular and vary in size from that of a millet seed to that of a lent l They are polygonal with definite borders and are slightly elevated, skin o hestnut colored and single or con fl ent. The lesions resemble erruca plana, are of lichenoid appearance a d are of hard consistency They are not scaly With the slightest trauma, they may give rise to blisters. They are usually located on the dorsal surfaces of th hands and feet with mosa c distribution but retain their individ ual haracter The intermediate skin may be lichen fied. On the palms and soles the condition appears s mila to punctat keratosi Occa ionally ther parts of the skin are invol ed Th na l a e opaque and fragile and there some hyperhi drosis and acron phyxia

Hi t logic examination of the ski how considerable hy perkeratosis, hypergranulosi nd hyperacanthos with d crete papillomatos There no parakeratosis or cellula culation a is bserved n erruca plana.

[4] Arch argent dermat 7 19 166, December 1957

The course of the disease is chronic. The lesions do not regress spontaneously but they display no degenerative changes. Treatment is of little value

Man 22, had a dermatosis which began at age 9 His father had had a profusion of warts since childhood, and a sister 9 had begun to show a similar skin picture during the past few months. The patient's verrucous lesions at first were localized on the dorsum of the hands and feet, but later extended to the legs and forearms and finally to the axillary folds and hairy skin. In the outer ear and temporal region



Fig. 48.—Papulosquamous lesions of auricular pavilion (Courtesy of Gonzalez, J L. Arch argent dermat 7 359 366 December 19 7)

there were dirty cru t (removed w th the curet) alternating with scabby papules (Fig 48) Flat p nhea l s red papules formed irreg ular plaques in the axillary inguinal and uperior thoracic regions. The nails were striated longitudinally The face was covered with an acne and biopsy of a skin lesion from the lor um of the hand showed hyperkeratosis, hypergranulosi and acanthosis, with pronounced papillomatosi n the derm Lymphocyt c nfiltration coincided with zones of epidermal parakeratosis. Biopsy of the retroauricular area showed similar hyperkeratos and granulosis. Papil lomatosis in the dermis was discrete, and lymphoh t ocyt c infiltra tion was perivascular Pilosebaceous connection were markedly hyperkeratotic. The sweat gland showed no changes. Dactyloscopy revealed interruption of the papillary lines.

Pityriasis Rubra Pilaris in Identical Twins, aged 10 1 reported by Erik A. Knudsen (Finsen Inst., Copenhagen) The lesions were mild, and the disease was diagnosed in 1 child only when the sister was also examined. There were no ther known cases of skin disease n the family

Leitner reviewed 152 cases of pityriasis rubra pilaris and concluded that the disease is *invariably hereditary* assum ng (as is probably correct) that there exist mild cases which are not recognized. Leitner s survey included genealogic ta bles of 15 famil es in which 2 o more cases occurred. These were analyzed by Ford, who concluded that the disease i probably always dominantly inherited it is, therefore to be expected in half the offspring of a d seased person and in half the members of an affected fam ly of sisters and brothers. Ford, however attached particular mportance to 3 tables in which the parents of those affected d d not ha e the disease though n other respect the familial tendency was bvious, t least in 2 of the cases. Ford suggested that this m ght arise by mutation or if heterogeneous carriers of th d sease were themsel es normal i.e dominance would be ncomplete *Mutation could be ruled out i 1 case and thus could not c* count fo all cases. Besides the d sease is so rare that the n mber of cases approaches the mutation frequency of the population One of Leitner s own cases was not diagnosed n til the patient was aged 40 despit frequent medical exam ination and objective symptoms Cases occurring in rela tives may ev dently be missed, and f th reason the solit ry cases ma perhaps also be *hereditary*

Extracellular Cholesterinosis (Kerl Urbach) Variant of Erythema Elevatum Diutinum, i discussed by J J Herzberg[1] (U Skin Clinic Hamburg) Histologic tudies of the patient reported on and of 2 ther suggested that extra ll la holesterinosis essentially a riant of erythema les tum diuti um The lipid nfiltration a secondary de *elopment w thout nosologic gn fica c*

Woman, 32, had ski disease for 10 years It started with urticaria porcellana on the extremities and buttocks which disappeared the ollowing year during pregnancy Four yea later the disease re curred with permanent, red to brown h olet nodes localized mostly on the extensor surface of the extremities At night and cold weather pains would recur in the nodes and the joint beneath them.

1 Deh J Dermat 70 27 29 January 58
ch Klin exper Dermat 205 477 496 58

Skin changes ... nd pigmentations with or without sc... would appear in the area of the n... ray treatment failed.

Physical examination was negative except for colpitis simplex and the mucosal and skin changes. The latter affected the buttocks, the area of the Achilles tendon, the anthelices and symmetrically the extensor surfaces of the upper arms down to the elbows, the knee area extending to the proximal part of the leg and the distal part of the thigh. The oral mucosa was also involved. The affected areas revealed brown polycyclic and sharply defined elevated efflorescences which varied from pea to larger than thumbnail size and occasionally coalesced to plaques. The surface of most lesions was scaly. Some were covered with bloody crusts while a few on the extensor surface of the fingers were ulcerated. Near these acute foci there were pigmented or depigmented scars and atrophic areas of old foci. The buccal mucosa on the left showed a lentil-sized, translucent whitish yellow tumor with superficial vascular markings.

During a 1 year hospital stay some of the nodes regressed spontaneously with pigmentation and with or without scar formation. In attacks, erythema exudativum like eruptions appeared on the extensor surface of the forearms and thighs. From time to time large painful, blood filled blisters developed rather suddenly within the area of the nodes. After removal of the blisters, a circumscribed necrotic area remained which, because of secondary infection, healed with scar formation. On the buccal mucosa and on the hard palate under the plates erosions and papules were observed.

Histologic examination of 3-day-old nodes revealed edema of the subepidermal connective tissues. The vessels of the superior plexus were surrounded by masses of polymorphonuclear cells situated in loose perivascula connective ti ue the latter consisting of broken up collagen fibers. These infiltrations contained also histiocytes, very few lymphoid cells and rarely an eosinophil cell. Macrophages, plasma elements and storage cells were absent. The capillaries were dilated, their endothelium wollen and the lumen filled with a reddish, homogeneous mass which was not a thrombus.

Examination of older nodes showed fibrin ma ses n the corneal layer and slight leukocytic infiltration between corneal and granular layers. The intercellula fi sures in the basal layer were widened a few basal cells showed vacuoles. The upper two th rd of the remaining cutis showed an exten ive cell n h ltrate ostly around the heavily damaged vessels, consi ting f polymorphonuclear leukocytes, rare eosinophil hi tiocyt c element and a f w lymphoid cells. Within the infiltrates ther were many nuclear fragments and in some areas macrophages. There wer few large cell with foamy plasma. No giant cells were observed. The number of capillaries was definitely increased, the r lumen filled, but not w dened, with leukocytes and red blood cells.

The structure of the connective tis ue wa altered. Sudan III ta n ing showed a partly d ffuse partly focal range-colored xtracellular collection of lipid. Very few large cell conta ned eddi h brown droplets in the cytoplasm

Of several forms of therapy tried, only ACTH by intravenous drip and cortisone influenced the skin eruptions and the joint symptoms favorably

Lipoid Granulomatoses of Subcutis were studied by H Lausecker[3] (Gen'l Hosp St. Pölten Austria) Lipoid granulomatosis denotes a morphologic entity occurring in various diseases. The Hand Schüller-Christian and Abt Letterer Siwe diseases and eosinophil granuloma of the bones are considered as various forms of the same basic disease especially n the Anglo-American literature. The latter is thought of as an nfectious granulomatous disease with remarkably phasi course. Diagnosis is based solely on the histologic changes. The linical picture may ary to a great de gree depending on the type of the disease and age of the foci.

Woman, 37 had many lipoid granulomatous nodules ppear in the subcutis over 2 years, accompanied by enlargement of the liver spleen and lymph nodes. X ray showed slight osteoporosis. Serum cholesterol levels were constantly at the upper limit of normal and the ratio of free cholesterol to cholesterol esters was about 1.5 During 4-yea follow-up, the symptoms and signs of the disease disappeared, probably independently of the treatment (diet, -rays) Thus lipoid granulomatosis proved transitory in thi patient. Histologically the nodes of the subcutis showed all four phases of lipoid granulomatosis and the round cell infiltrate consisted almost exclusively of plasma cells.

Invol ement of the lymph nodes splee nd liver suggest that this pat ent had a generall ed d sease that also affected the subcutis The author suggests that lipoid granulomato s is an fectious-allergi disease proces n patients with an abnormal con titution

Case of Infantile Xanthomatosis is described by Aldo Leoni d S l so B essanin (Univ of Padua)

Boy aged 15 months, poorly developed, had lesion in the scrotum at birth Several months later papular and nodular lesions appeared on the scalp then on the forehead, temples, back, chest and extremities They ere heat to lentil sized, slightly elevated, round ith clearcut borders, parenchymatous, fa colored, isolated and ithout inflammation. Lipid findings were normal.

Histologic study revealed a slightly thinned epidermis with marked flattening of the intercapillary elements and the dermal papillae. The malpighia layer w altered and the horny layer slightly thickened. The superficial layers of the skin showed intense reticuloendothe lial proliferation, with foam cell rich in protoplasm and large nuclei that stained easily w th odan III I the infiltrate were numer

3) Hautarzt 3:149 April, 1952
) Minerva dermat 31:236-239 June, 1952

Skin changes would come and go leaving behind pigmentations with or without scars. Occasionally "bloody blisters" would appear in the area of the nodes, with considerable pain. X ray treatment failed.

Physical examination was negative except for colpitis simplex and the mucosal and skin changes. The latter affected the buttocks, the area of the Achilles tendon, the anthelices and symmetrically the extensor surfaces of the upper arms down to the elbows, the knee area extending to the proximal part of the leg and the distal part of the thigh. The oral mucosa was also involved. The affected areas revealed brown polycyclic and sharply defined elevated efflorescences which varied from pea to larger than thumbnail size and occasionally coalesced to plaques. The surface of most lesions was scaly. Some were covered with bloody crusts while a few on the extensor surface of the fingers, were ulcerated. Near these acute foci there were pigmented or depigmented scars and atrophic areas of old foci. The buccal mucosa on the left showed a lentil-sized, translucent whitish yellow tumor with superficial vascular markings.

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Examination of older nodes showed fibrin masses in the corneal layer and slight leukocytic infiltration between corneal and granular layers. The intercellular fissures in the basal layer were widened; a few basal cells showed vacuoles. The upper two thirds of the remaining cutis showed an extensive cell rich infiltrate mostly around the heavily damaged vessels, consisting of polymorphonuclear leukocytes rare eosinophil histiocytic element and a few lymphoid cells. Within the infiltrates there were many nuclear fragments and in some areas macrophages. There were few large cells with foamy plasma. No giant cells were observed. The number of capillaries was definitely increased their lumen filled, but not widened, with leukocytes and red blood cells.

The structure of the connective tissue was altered. Sudan III staining showed a partly diffuse partly focal orange-colored extracellular collection of lipid. Very few large cells contained reddish brown droplets in the cytoplasm

the hyalinized collagen surrounding these fibers and the particles of calcium were not digested. Elastic tissue from normal skin and ligamentum nuchae exposed to elastase showed changes identical with those seen in the biopsy specimen. Control collagen fibers were unaltered.

Darkfield examination of the microincinerated sections showed heavy deposits of the white ash characteristic of calcium and/or magnesium in the mid and lower dermis. In the involved area of the dermis the white ash existed in irregularly dispersed large clumps. Occasional rod-shaped fibers, some sharply angulated, were found in and adjacent to the large calcium clumps. All these discrete fibers were sharply outlined with the white ash and appeared to contain granules that reflected light in a manner indistinguishable from the large masses.

In sections viewed by electron microscopy the appearance of the altered fibers was typical of elastic tissue and did not resemble collagenous tissue. These fibers were surrounded by and mixed with fibers with the 640 A. periodicity typical of collagen.

On the basis of these findings the authors believe that the fibers in pseudoxanthoma elasticum which have an affinity for the established elastic stains and which resemble elastic tissue in hematoxylin and eosin stains are actually elastic fibers. These altered elastic fibers may act as foreign material evoking an inflammatory and giant cell reaction, calcification and eventually an increase in collagenous fibrous tissue in the involved portions of skin. Results of this study do not exclude the possibility that both elastic and collagenous fibers are primarily involved in this disease though this seems much less likely.

► [Some authors are of the opinion that the fibrous elements affected in pseudoxanthoma elasticum are collagen fibers. Shaffer, Copelan and Beerman (A.M.A. Arch. Dermat. 76:622, 1957) called attention to the triad of pseudoxanthoma elasticum, Paget's disease and angioid streaks and reported a case of pseudoxanthoma elasticum associated with calcinosis of the subcutaneous tissues and widespread calcification of the major blood vessels.—Eds.]

Idiopathic Atrophoderma of Pasini and Pierini. According to Orlando Canizares, Perry M. Sachs, Leon Jaimovich and Victor M. Torres[4] (New York Univ. Post-Grad. Med. School and Bellevue Hosp.) progressive idiopathic atropho-

(4) A.M.A. Arch. Dermat. 77:42-60, January, 1958.

ous foreign body giant cells and some round, empty spaces bordered by a crown of flattened cells thought to be newly formed transected endothelial tubules. In the deep layers the sudanophil elements were less numerous with infiltrates of lymphocytes. The connective tissue collagen in the lesion had almost disappeared and showed homogenization at the periphery

Because of the absence of hereditary or familial elements, of involvement in other organs or tissues and of primary systemic processes in the reticuloendothelial system the diagnosis was restricted to the group of disseminated xanthomas of infancy with normal lipid values. The authors diagnosis was infantile xanthomatosis although the case was much like nevoxanthoendothelioma Congenital infantile xanthomatosis is rare in Italy this being one of the few cases reported so far

Studies on Nature of Abnormal Fibers in Pseudoxanthoma Elasticum. Thomas J Moran and Albert I Lansing[4] (Univ of Pittsburgh) studied involved skin from a typical clinical and histologic example of pseudoxanthoma elasticum by standard histologic methods elastase digestion microincineration and electron microscopy

Histologic examination of hematoxylin-eosin stained slides revealed the characteristic changes of pseudoxanthoma elasticum in the mid and lower dermis. An irregular but fairly sharply outlined nodular band of altered often hyalinized, fibers of bundles was found in whorls or irregular streaks around particles or clumps of blue-staining material resembling calcium Sections stained with orcein showed many varying sized fragmented, often thick and irregular red fibers which were indistinguishable from elastic tissue elements These were principally in the calcified portions and were surrounded by wide bundles of tissue resembling collagen

Observation of the sections after digestion with elastase showed the characteristic change of elastic tissue The fibers staining red with orcein assumed a prominent transversely segmented, striped or ladder appearance as they underwent partial dissolution (45 minutes) After 2 hours almost all these fibers in the elastin-covered areas had disappeared, though a few thick fibers were still seen These also showed a striped or segmented appearance The involved fibers in areas protected from elastase action were unchanged and

(4) A.M.A. Arch. Path. 65:658-696, June 1958

Differential Diagnosis between Morphea and Idiopathic Atrophoderma of Pasini and Pierini

Morphea	Idiopathic Atrophoderma of Pasini and Pierini
Sex	
More common in women	More common in women
Age at onset	
Mostly between 20 and 50	Teens or early twenties
Location	
Extremities, especially lower trunk, face and neck	Chiefly trunk back always affected hands, feet and face almost invariably free
Duration of activity	
Average 3—5 years	Progressive 10—20 years
Clinical appearance	
At onset thickened, indurated, pink or mauve colored patches	At onset soft, depressed with cliff drop border bluish brown or bluish violaceous patches No lilac ring
Later center pales, becomes ivory colored with peripheral "lilac ring" unpinchable, attached to deeper structures patches seldom run together	Later patches vary run together forming larger patches large veins faintly visible areas of sclerodermatous changes may appear in center
Course	
May disappear spontaneously without leaving sequelae or may leave slightly atrophic hyperpigmented patch	Usually progressive until reaching standstill there is no involution of lesions occasionally concomitant lesions suggesting morphea in edematous stage involute into soft, depressed bluish plaques
Histopathologic characteristics	
Edema of collagen which may extend in upper cutis to deeper cutis pronounced sclerosis elastic tissue changes absent or minimal if present, appear late	Edema of collagen in mid- and deep cutis no sclerosis elastic tissue changes concomitant with edema in deep cutis deep vessels engorged in patches presenting pronounced edema of collagen simultaneously with elastic tissue changes when the former subsides, the latter remains

cially the back. The fac hands and feet are almost invariably free (3) Individual lesions ary from a few centimeters in diam ter to large pat hes. (4) The lesions are bluish violaceous or browni h blue and are depressed from the surrounding skin (Fig 49) w th a sharp abrupt cliff drop border or a gradual lant. (5) There is faint blurred visibility f the deeper blood vessels. (6) The surface of the lesions is mooth and normal except for color (7) No induration is palpable. (8) The skin around the pat hes is normal. (9) If

derma of Pasini has not received attention as such in the American dermatologic literature. During the past 20 years Pierini has observed over 50 cases and has made invaluable contributions to the knowledge of this condition. For this reason the authors suggest the term "idiopathic atrophoderma of Pasini and Pierini" for this peculiar cutaneous atrophy.

They present 5 cases, 2 in males and 3 in females. Onset

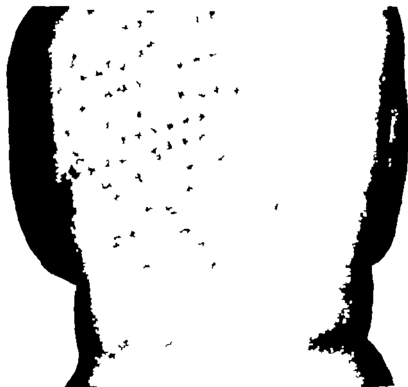


Fig. 49.—Multiple depressed patches on back of patient. Two show sclerodermatous changes. (Courtesy of Canizares, O., et al.: A.M.A. Arch. Dermat. 77:42-60, January 1958.)

was in the teens or early twenties. The lesions were on the trunk, always affecting the back. In 4 cases the lesions were asymptomatic; 1 patient had occasional tingling or sensation of warmth. The slow, progressive course ranged from 4 to 15 years. Although no complete involution was observed, there was an apparent spontaneous arrest in 2 cases.

The clinical characteristics of idiopathic atrophoderma of Pasini and Pierini include the following: (1) Onset is in the teens or twenties. (2) The trunk is chiefly affected, espe-

preparations and cultures from the inguinal lesion were negative. Biopsy of a neck lesion showed familial benign chronic pemphigus.

Of the 6 patients, 2 had familial history of the disease. Four had exacerbations in hot weather Although this disease is considered rare in the Negro 4 of the patients were Negroes System c administration of antib otics was beneficial in 5 of th patients.

► [One must be constantly alert for the "atypical" features of this disease because sometimes the diagnosis will hinge on their recognition. Fortunately the biopsy is usually diagnostic —Eds]

Problems and Results of X-ray Examination of Skin and Its Diseases II. X-ray Findings in Pathologically Changed Skin are discussed by Gotthard Lemke (Univ Skin Clinic Freiburg) I diagnostic x ray studies of the skin the subcutaneou fat tissues serve as physiologic contrast mediums. The fine tructure of the normal skin can be visualized by soft x-rays if ts components are of macroscopic size. The kin changes in various dermatoses can be demonstrated by x rays because f *differences in volume baorption* and density Skin diseases not accompanied by these differences cannot be visualized by x ray

X ray pictures present *only* the *conditions at a given moment.* Serial follow-up films, however indicate the changes taking place over a period of time. Serial films reveal not only gros kin hanges but also transient or clinically insig ficant *ymptom such as wheals in urticaria.*

I several skin diseases characteristic and often pathog nomonic x ray picture is observed which allows a diagnosis without knowing the clinical or other data In certa n in tances x-rays reveal changes which are not suspected by routine l cal stud es Thus the wheals in acut and also in chronic relapsing urticaria re represented in the x rays by hanges n th eticula etwork of the ubcutis besides th clinically u pected broadening of the cutis l ne. This is observed regula ly and ndependently of the size and age of the wheal In lder larger wheals it is even poss ble to dem n trat m scular m l ement *in the form of ill-defined and* loosened muscular fascia. Th would ggest that not only the capillaries d the smallest essels of the cutis are in ol ed but lso those the adjacent layers of the subcutis Sim la ly changes ca be detected regularly in the subcuta neou fine tructure erythema exudativum and in psoriasis

7) Arch. klin. u. exper. Dermat. 207 374-414, 1958

sclerodermatous changes appear they develop years later within the patches of atrophy (Fig 49) or simultaneously in separate lesions In some cases lesions with clinical appearance of morphea have gradually developed this atrophic picture

The significant microscopic features of the cases cited were edema of the collagen bundles of the deep cutis and accompanying irregular clumping and loss of elastic tissue in this area The fat and epidermis were uninvolved.

Although the lesions in idiopathic atrophoderma of *Pasini* and *Pierini* may show morphea like features they are not believed to be the disease entity morphea or scleroderma Chief points of differential diagnosis are shown in the table

► [Atrophic lichen planus must be considered in differential diagnosis. *Here the atrophy may be sharply defined with a cliff drop border and some pigmentation may remain.*—Eds]

Atypical Features in Familial Benign Chronic Pemphigus were observed by Thomas W Lyles John M Knox and J B Richardson[6] (Baylor Univ) in 6 patients

CASE 1 —Man 55 Negro had hyperkeratotic verrucous lesions on the lower legs. The neck axillae, popliteal fossae groin and sacral area showed scattered vesicles surrounded by whitish, macerated papules and crusts. Biopsies from the axilla, groin and a verrucous leg lesion revealed the typical intraepidermal bullae of familial benign chronic pemphigus.

CASE 2.—Woman, 22 Negro had white-topped papular lesions on the external genitalia, which apparently had been precipitated by pregnancy Biopsy showed familial benign chronic pemphigus. The eruption disappeared after elimination of leukorrhea that occurred post partum.

CASE 3.—Woman 76, Negro had pemphigoid vesicopustular lesions involving the frontal and preauricular hairline in addition to biopsy-confirmed lesions of familial benign chronic pemphigus in the axilla. It was theorized that a pyoderma predisposed to development of lesions in such an uncommon site but it was not possible to determine whether the pyoderma was primary or secondary

CASE 4 —Woman 55 Negro had widespread lesions involving the neck, antecubital fossae axillae and thighs. The distribution and clinical appearance suggested neurodermatitis dissеminata, but biopsy showed familial benign chronic pemphigus

CASE 5 —Man 42, white had lesion with erythematous vesicular borders and clearing centers resembling tinea corporis. Biopsy showed familial benign chronic pemphigus

CASE 6.—Man, 51 white, had annular erythematous scaly papulovesicular lesions on the neck and shoulders and a lesion in the groin suggesting monilial intertrigo. Repeated potassium hydroxide

(6) A.M.A. Arch. Dermat. 78:446-453, October 1958

In the erythema nodosum group the cutis s distinctly thickened roentgenographically in the area of the lesion. Its lower border is indistinct, and the cutis passes gradually into a network of fairly coarse fibers. Small meshes are bound by coarse threadlike septa. Peripherally and toward the deep layers the lesion merges successively into normal tissue with sparse and slender septa. The lower margin of the cutis nd ts transition into septa resembles a fringed edge of a piece f cloth or the surface of a coarse blanket. The clearly visible septa probably correspond to the histologically changed connective tissue areas i cluding the vessels. Small areas of fatty tissue observable between them are fairly reg ular n size nd shape

In the erythema induratum group the thickened cutis at the site of the lesion shows a distinct, well-discernible line of separation from the subcutis. Histologically the septa are slender and less marked and, therefore, do not appear as distinct as the septa n the erythema nodosum group The subcutis appears diffusely increased n density as in edema with infiltration. Connective tissu of regular appearance can no longer be seen marked, dense bands without regularity are occasionally observed, and these possibly correspond to the course of the subcutaneous vessels.

► [It is certainly of interest that the authors are able to discern so much soft tissue detail from x-ray studies of cutaneous and subcutaneous tissues. —Eds.]

Rosacea Like Tuberculid of Lewandowsky W G van K tel* (Uni of Amsterdam) studied 55 patients with osa ea papulosa and papulopustulosa (rosacea l'ke tubercu lid) All had thorough physical examinations and one or mo biopsies In 37 cases rosacea existed without peculiar l ical or hi tologic characteristics and without an active tuberculous focus or a clear h story of tuberculous infect on. The Mantou test t 1 1000 was pos tive in 19 of these cases d egativ 17

I (patients the diagnos s of rosacea like tuberculid was cons dered on clinical ground (lat ral di tribution on the heek and neck d/or results of diascopic inspection) In f these the local zation h fted from lateral to medial in the course of the disease and d ascopy became negative. In 1 patient two different types of papules were found, one

* Dermatologica 11 201 214, March, 1955

vulgaris These changes are not seen on clinical or histologic examination

All forms of cutaneous subcutaneous tuberculosis studied show common x ray features In the individual case, usually a certain sign is in the foreground which is of diagnostic help. X rays also reveal the quick clearing of deep infiltrations.

X rays may assist in assessment of the pathogenic role of vessels. Besides perivascular infiltrations changes in the vessel wall can also be demonstrated In erythema nodosum, the phlebitic and periphlebitic infiltrations appear as poorly circumscribed broadened vascular shadows Thickened vessel walls are demonstrated in necrobiosis lipoidica, panarteritis nodosa and circumscribed and progressive scleroderma. In periarteritis nodosa vascular changes can be shown by x rays even before appearance of clinical symptoms.

Roentgenographic Studies of Cutaneous and Subcutaneous Infiltrates in Erythema Induratum and Erythema Nodosum are reported by C G Leczinsky and O Mattsson[1] (Karolinska Hosp Stockholm)

METHOD.—The skin eruptions were recorded with a tangential beam. To achieve this, an indicator was applied to the center of the affected skin surface. The central beam could be easily adjusted in relation to the efflorescence under fluoroscopic control with the image intensifier by means of a special variable diaphragm, the irradiated field could be reduced selectively to a minimum Thus the amount of secondary radiation and the so-called extrafocal radiation were also reduced, with resultant improvement in the quality of the image Recordings were made on a nonscreen film, using 40-50 kv

Twenty cases of panniculitis of the lower legs were studied. Typical x ray appearances were found in two main types of subcutaneous changes which the authors call the erythema nodosum and erythema induratum groups Included in the former group were typical cases of erythema nodosum some cutaneous forms of periarteritis nodosa and erythema nodosum migrans and perstans. The erythema induratum group consisted of tuberculous and nontuberculous erythema induratum Darier s subcutaneous sarcoid Weber Christian disease in certain stages and several similar affections. Besides the erythema induratum and nodosum groups an intermediary group was also seen Of the 20 cases 7 were erythema nodosum in type 9 induratum and 4 intermediary

(1) Acta radiol. 49 193 204 March, 1958.

fection decreased during the 6 year of th study Whereas n 1951 53 73% of 49 children were tube culm positive, in 1954-56, thi proportion fell to 51% of 56 cases. Of the 65 children with positi e tuberculin tests, 46 had cl cal and r diologic ev dence of a recent and active tuberculous proc es a d 19 the only evidence of the tuberculous infection wa the pos ti e kin test The proportion of hildren having acti e primary tuberculosis wa 55 % n the first 3 years and 34% in the second period. Of the 46 child en with active pri mary tube culosi 10 had important tuberculous complica tion w thin 9 mo ths of the appearance of erythema nodo-um tuberculous meningitis in 3 bronchopneumonia in 1 rthriti of the hip n 1 pleural effusion in 3 and pustular conjuncti itis in 2.

F e children exhibited erythema nodosum after BCG vac cination, and in 4 of these the eruption occurred at the tim of tuberculin conversion. Nevertheless, n 3 of the children there was also evidence of streptococcic infection at the time the eruption appeared.

Of 35 patient whose tuberculin test and radiographs wer negativ at the time of erythema nodosum 17 had a sore throat within 2 weeks before the eruption. In 10 of these l borat y e idence of a beta hemolytic streptococcic infec tion was obtained. I 19 children no investigations were perf rmed to pro a possible streptococcic etiology In most f the tuberculou patients no further in estigations were carried out aft r evidence of tuberculosis was found. How ever erythema nodosum was p eceded by sore throat in 15 nd st eptococcic nfection was demonstrated in 5

These findings indicate that tuberculosis is still n impor tant etiologic factor in erythema nodosum in children but ts importance is teadily decreasing As BCG accinations a e increasing in umber it will have to be considered as a po s ble cause in cases of erythema nodosum The true inci-lence of treptococcic tiology will not be known until all cases are investigated routinely by throat swabs and estima t on of ant trept lysin titers When this i done many cases of erythema nodosum will probably be found wh ch mul tiple factors operate

showing no reaction to diascopy and the other showing a reaction. Changes in localization and in diascopy occurring in the course of the disease prove that clinical differentiation between rosacea and rosacea-like tuberculid is impossible. In half the patients with clinical findings suggestive of rosacea-like tuberculid no evidence of a tuberculoid structure was found in microscopic sections of the papules. Of 49 clinically normal rosacea patients 5 showed a clear tuberculoid structure and 4 showed signs of such structure. Thus tuberculoid structures are not rare in rosacea papulosa, and histology cannot be conclusive in differentiating rosacea and rosacea-like tuberculid.

No connection was found between the presence of tuberculoid infiltrates and the results of examination for tuberculosis. However, 3 patients with clinically normal rosacea and no evidence of tuberculoid structure histologically had an active tuberculous focus or a definite history of such infection. Since rosacea may be present with tuberculous lesions in other parts of the body, examination for tuberculosis is of little value in differentiating between rosacea and rosacea-like tuberculid.

Neither clinical nor histologic examination, separately or combined, constitutes an effective criterion for distinguishing rosacea from so-called rosacea-like tuberculid. Rosacea-like tuberculid of Lewandowsky is not to be regarded as a separate disease and must be considered identical with rosacea papulosa or rosacea papulopustulosa.

► [There are reasons for abandoning the term "rosacea-like tuberculid of Lewandowsky," e.g., those first pointed out by Snapp, who suggested the name "Lewandowsky's rosacea-like *eruption*," and now those given by van Ketel. There is a very small group of cases which clearly show apple jelly nodules clinically and tuberculoid structures histologically and which also have some features of rosacea. These cases should be considered "lupus miliaris disseminatus faciei" or "micropapular tuberculid." The remainder should be classified with rosacea or acneiform eruption or whatever other entity they fit in best.—Eds.]

Changing Etiology of Erythema Nodosum in Children. Among 105 consecutive children with erythema nodosum seen during 1951-56 John Lorber[1] (Children's Hosp., Sheffield, England) found a positive tuberculin test as a result of natural infection in 65 (62%). Incidence of tuberculous in

(1) Arch. Dis. Childhood 33:137-141, April, 1958.

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(1) Arch. Dis. Childhood 33 137 141 April, 1958

C. wernecki into the palms, soles and glabrous skin of 2 human volunteers were unsuccessful.

► [Here is another of the few pigmented lesions of the palms other than nevi that should be considered in differential diagnosis.—Ed.]

Extensive Trichophyton Infections of about 50 Years Duration in Two Sisters are reported by F. Blank, P. Schopflocher, P. Poirier and J. L. Riopelle (McGill Univ.). The eruptions were widely distributed over the body and resulted in alopecia totalis in both patients. Many deep granu-



Fig. 50.—Granulomatous lesions on back. (Courtesy of Blank, F., et al.: Dermatologica 115:40-51, July, 1957.)

lomatous lesions were present in 1 case only (Fig. 50). It is difficult to explain why the dermatophyte invaded the dermis in 1 sister and under apparently similar conditions restricted its pathogenic activities to the epidermis in the other. Special, yet unknown conditions must prevail so that the fungus, a highly specialized parasite of the keratinized layers of skin, nail and hair, becomes capable of living and multiplying in the dermis. These special conditions apparently are rarely met, since dermatophytosis is common but invasion of the dermis is rarely reported.

(3) Dermatologica 115:40-51, July, 1957.

11 FUNGOUS INFECTIONS

Tinea Nigra Palmaris Disorder Easily Confused with Junction Nevus of Palm is described by J Graham Smith Jr Wiley M Sams and Frank J Roth Jr[2] (Univ of Miami) *Tinea nigra palmaris* is caused by the fungus Cladosporium wernecki In the western hemisphere nearly all reported cases have involved the palms however cases involving other areas of the body such as the neck or thorax, do occur The asymptomatic macular lesions neither elevated nor scaly are brown or black appearing as an India ink or silver nitrate stain The disease must be differentiated from nevi, contact dermatitis pigmentation of Addison s disease and drug eruptions The disorder responds readily to local therapy with keratolytic agents such as salicylic and benzoic acids The authors report 2 cases. Both were mistakenly diagnosed as nevi 1 by experienced plastic surgeons and the other by competent dermatologists

CASE 1—Woman 55 who had not been out of Dade County Fla., for 10 years had an asymptomatic, brown, macular lesion on the left palm. It gradually enlarged during 2½ months. It was not elevated or scaly and measured 2×2 cm. Microscopic examination of a scraping in 10% potassium hydroxide revealed branching hyphae Cultures were identified as C wernecki The patient was treated with 3% salicylic acid ointment The lesion completely disappeared except for residual erythema, in 3 weeks.

CASE 2.—Physician s daughter 5 had a small asymptomatic 8×10-mm pigmented lesion on the right palm. The lesion looked like café-au lait pigmentation and was of normal texture No mycologic examination was made and the lesion was excised, with a preoperative diagnosis of pigmented nevus Microscopic examination revealed hyphae and spores in the upper stratum corneum and a minimal perivascular infiltrate of lymphocytes and histiocytes in the upper dermis. The pathologic picture was considered diagnostic of tinea nigra.

Including these a total of 3 cases of tinea nigra palmaris acquired in Florida and 4 from Texas have now been reported in the United States. Case 1 is the first reported in the United States in a patient over age 12 Attempts at experimental reproduction of the disease by inoculation of infected scales from the first patient and material from a culture of

(2) J.A.M.A. 167 312 314 May 17 1958

in 9.4% of abnormal asymptomatic interspaces and in 64.7% of those with symptoms. The association of coagulase-positive staphylococci with the presence of symptoms was statistically significant. There was no significant variation in the distribution of other bacteria in either the 1st or 4th interspaces of patients with normal interspaces, asymptomatic abnormal interspaces and symptomatic interspaces.

Recovery of both pathogenic fungi and staphylococci from the same interdigital space occurred in 11.4% of subjects. Though this association was found in only 2.2% of normal interspaces and 3.1% of those without symptoms, it occurred in 47.1% of those with symptoms. This finding was also statistically significant. A pathogenic fungus was found with a beta hemolytic streptococcus in 1 person with abnormal skin but no symptoms and in 1 with symptoms.

The results suggest that clinical symptoms of tinea pedis are the outcome of the association of pathogenic fungi and staphylococci even in cases without acute inflammation and which are usually regarded as purely mycotic in origin. If this is so, some alteration in treatment of athlete's foot might be worth considering. In subjects with extensive secondary infection of the foot, a preliminary course of mild treatment to reduce inflammation before the application of fungicides is usually advised. It is possible that a two-stage treatment in all forms of athlete's foot with subjective symptoms, the first stage directed specifically toward the staphylococcus and the second toward the fungus might produce a more satisfactory result.

► [This study reveals that just as pathogenic fungi can often be found on clinically "normal" feet, so can coagulase-positive staphylococci also be recovered. The question, of course, is whether the staphylococci contribute to the activity of the fungi to produce clinically discernible changes or whether the staphylococci merely grow in the suitable terrain prepared by the fungi. We would suspect the latter explanation to be correct, as appropriate antifungal therapy alone is usually adequate to care for the infection. The availability of antifungal antibiotics, such as griseofulvin, which is effective on oral administration, may help to answer this as well as many other hitherto unanswerable questions in the field of superficial fungous infections.—Eds.]

Fungous Disease as Complication of Steroid Therapy is discussed by Robert F. Burns[4] (Henry Ford Hosp.). There is general agreement that systemic steroids promote dissemination of deep fungous infections in laboratory animals. However this observation cannot necessarily be applied to

4 A.M.A. Arch. Dermat. 77:666-699, June, 1958.

A biopsy specimen from the patient with granulomatous lesions showed granulomatous reactions within the entire cutis Short and long septate hyphae were found in large multinucleated giant cells and interstitially Hyphae could not be demonstrated in small foci of necrobiosis. No keratinous material could be detected in any section The fungus may have penetrated through the hair follicle into the dermis. *After it had digested all the keratinous material present, the dermatophyte became adapted to the changed ecologic conditions, i e to living without keratin in the dermis.*

Trichophyton epilans was isolated in both cases The cultures isolated from the deep granulomatous lesions varied slightly in some colonial and microscopic features from those isolated from scaly eczematous lesions in the same patient and in her sister The authors do not believe that two species were involved but that the alteration in the fungus morphology was the result of adaptation to a keratin-free environment.

Oral administration of potassium iodide and x ray treatment caused remarkable regression of the granulomatous lesions *in the first patient.*

► [It would have been interesting to know whether any abnormality in the anatomy or physiology of the skin was present in these 2 sisters and whether there was any family history of such abnormalities This might have explained the coincidence of persistent and extensive fungous infection in both sisters as it did in the patient with widespread T rubrum infection studied by Baer and Muskatblit (Arch Dermat & Syph 56 834 1947) —Eds]

Search for Presence of Pathogenic Bacteria and Fungi in Interdigital Spaces of Foot of 175 subjects was carried out by Mary J Marples and Margaret J Bailey[4] (Univ of Otago) In 45 the interdigital spaces showed no abnormality clinically though 13 had had athlete's foot previously In 96 there was *asymptomatic maceration or scaling in the 4th interdigital space* or in other spaces besides the 4th In 34 subjective symptoms were present and one or more interdigital spaces showed maceration scaling or fissuring

Pathogenic fungi were demonstrated in 20% of all subjects Fungi were present in 8 9% of those with normal interdigital spaces in 12 5% of those with asymptomatic abnormal spaces and in 58.8% of those with symptoms Coagulase-positive staphylococci were isolated from 20% of the subjects They were *found in 8.9%* of normal interspaces

(4) Brit. J Dermat. 69 379-388 November 1957

that such treatment produces tendency to development or to flare-ups of superficial fungous infections.—Eds.]

Comparative Studies of Special Mediums for Identifying Candida Albicans from Other Candidas and Molds. Many laboratory procedures have been proposed, but the most simple, rapid and inexpensive technic for identifying C. albicans is to demonstrate chlamydospore formation. This diagnostic spore formation can be induced on corn meal, rice infusion and bactochlamydospore agars. A culture medium proposed by Nickerson contains as an active ingredient a complex polybismuth sulfite.

Bahram Sina and Frederick Reiss (New York Univ. Post Grad. Med. School) used a known strain of C. albicans and 30 strains of candida species freshly isolated from lesions of the skin and mucous membranes in a comparative study of these culture mediums. The known strain of C. albicans grown on rice agar formed chlamydospores in 5 days, whereas it required 10 days on corn meal agar and bactochlamydospore agar. None of the strains of C. krusei, C. parakrusei, C. guilliermondi, C. stellatoidea, C. tropicalis and C. pseudotropicalis which were grown on these mediums produced chlamydospores. Candida albicans occasionally produced chlamydospores as early as the 2d day of incubation on rice agar but not on the other mediums. Of the 30 strains of C. albicans, all produced chlamydospores on rice agar, 23 on corn meal agar and only 20 on bactochlamydospore agar.

Nickerson's agar is not recommended as a routine procedure for identification of C. albicans since a number of species not belonging to genus Candida are also capable of reducing bismuth and forming jet black or brown colonies. Rice infusion agar is most suitable for identification of C. albicans.

Rapid Serologic Differentiation of Candida Albicans from Candida Stellatoidea. The commonly accepted criterion for routine identification of C. albicans in culture is the production of chlamydospores on special mediums. Though satisfactory for most purposes, identification by means of chlamydospore agars is inexact, since strains of C. stellatoidea, a

( ) J. Invest. Dermat. 29:243-247, October 1957.

man not only because of the difference in response between species but because the steroid dosage in animal experiments is often far in excess of that used in clinical medicine.

Clinically there is good evidence that there has been some increase in secondary systemic fungous disease in the past 10 years or so That steroids are the sole cause of the increase need not follow In the same decade broad-spectrum antibiotics and the cytotoxic agents have come into wide use Few of the recorded cases in which systemic fungous disease followed steroid therapy were of purely cutaneous disease In the main patients had blood dyscrasias, lymphomas cancers diabetes widespread burns and similar diseases with profound systemic implications which would be expected to influence the immune mechanisms unfavorably Besides the patients received not only steroids but antibiotics or cytotoxic agents or both

Increase in mortality from secondary fungous infections lies chiefly in systemic moniliasis aspergillosis and histoplasmosis with some increase in mucormycosis and cryptococcosis Coccidioidomycosis and blastomycosis are not considered to have increased in frequency with steroid administration There is also considerable evidence that large doses of steroids may have a virulence-enhancing effect on human superficial mycoses

An awareness of the risk of dissemination of fungous disease by steroid therapy is necessary but the danger is not so great that essential treatment should be withheld Good medical precepts should be followed and a complete examination including chest x ray should be performed before major steroid therapy is initiated If this is done and follow up examinations are reasonably thorough there i little chance of serious trouble Despite these precauti n y temic fungous disease will develop n rare occa ion and this must be counted as a calculated ri k of steroid therapy

Superficial mycotic infection should alw ay be br ught under control before the start of treatment if fea ible if n t active treatment should be carried n during y temic te roid therapy

► [In our extensive experience with long term ystemic and t pical corticosteroid therapy during the past 8 years w have seen no evidence

that such treatment produces tendency to development or t flare-ups of superficial fungous infections — Ed.]

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( ) J Invest. Dermat 29 343 347 October 1957

saprophyte share with C albicans the ability to form these spores Morris A Gordon[7] (Med College of South Carolina) describes a simple staining procedure for differentiation of these organisms. Fluorescein labeled specific antiserum is applied to smears from culture or clinical material, which are then examined by ultraviolet microscopy for fluorescent yeast cells

Although a definitive evaluation of the fluorescent antibody technic as a routine tool for differentiation of C. albicans from C stellatoidea must be preceded by work with many more strains of the organism the method is expected to show about the same specificity and perhaps greater sensitivity than the precipitin test described by Trimble The fluorescent method has the advantages of extreme rapidity and simplicity and can be applied to small numbers of cells—even a single cell viable or not in pure or mixed culture The technic is also applicable to identification and differentiation of yeast cells directly in smears from suspected mycotic lesions e.g., those of the vagina In vitro C albicans is readily differentiable from the components of the mixed normal vaginal flora with the exception of C tropicalis. This cross reaction may possibly be eliminated by further serologic studies. In preliminary work with clinical specimens, C albicans has been shown to stain intensely with the appropriate conjugate in oral mucosal smears from cases of thrush

Atypical Favus of Scalp Report of Two Patients with Seborrheic Form is presented by Oscar L Heim (Philadelphia) The distinction between typical and atypical favus of the scalp according to Sabouraud depends on the presence or absence of scutula but in many incidences miliary or minute scutula are found in the atypical form One of the author's patients was a white soldier 19 who represented a sporadic case of favus from western Arkansas The other was a white soldier 22 who contracted the disease in a known endemic area in eastern Kentucky Both patients had areas of partial alopecia in the scalp covered with layers of grayish white scale (Fig 51) After removal of the scales and after thorough search, miliary scutula were found Each scutulum was round about 3 mm in diameter pierced in its center by a parasitized hair and with n[illegible] nca its [illegible] n

(7) J Invest. Dermat 31 123-125, August, 1958
(8) A.M.A. Arch Dermat 76 40 751 December 19

perior urface Th color wa pal yellow which changed t a golden yellow with a drop of 70% alcohol Affected hairs were dull greeni h and fluorescent under W ood l ght Potassium hydroxide preparations and cultures revealed Trichophyton (Achorion) schoenleini

The seborrhe c form of favu i not easily recognized un less it i kept in mind but f the scalps of all patient who



[illegible] 3.—Large plaque of [illegible] on [illegible] vertex of scalp [illegible] [illegible] Miliary scutula were seen only after scales were scraped away. [illegible] hairs in plaque. (Courtesy of [illegible], O E A.M.A Arch Dermat 7 [illegible] December [illegible]937.)

present linical ign of seborrhea s cca, seborrheic derma titis psoria and tinea amiantacea are exam ned for minute scutula a d a Wood l ght i used to detect fluorescent hairs fewer m takes will be mad in diagnosis. Both of these pa tient wer seen over period f years by a numbe of physi cian before a diagno si of favus was establi hed

In man, f vus of the scalp irrespective of the clin cal form is caused by T (Achorion) schoenleini. Though favus located elsewher on the body may be caused by this fungus su h favus can occa ionally be due to other dermatophytes

Favus is not considered highly contagious in countries in which hygienic standards are reasonably high, but epidemics may occasionally occur in hospitals and schools. Total epilation with x-rays is indicated in treating favus of the scalp. Preliminary treatment directed to destruction of scutula is important and close surveillance of the scalp after epilation is necessary to prevent recrudescence.

Comparative Studies on Technic of Fungus Demonstration in Skin and Nail Mycoses. With Special Reference to Staining with Parker Ink. K. Enderlin[9] screened 134 employees of the public baths in Zurich for fungous diseases of hand, foot and nail. Fungi were sought in the same specimen by culture and microscopically with the standard xylol method and with a new technic using potassium hydroxide and Parker ink.

Method.—The specimen (scale, nail fragments, hair) is placed on a slide, covered with a cover glass and impregnated with a mixture consisting of 1 part blue-black or blue Parker ink (blue-black Parker ink 51 Superchrome) and 9 parts 5-10% potassium hydroxide (nails require the higher concentration). The slide is then placed into a humid chamber for 24 hours. Microscopic studies, even under low power, reveal the blue stained fungous filaments.

The Parker ink method was the most successful in detecting fungous filaments. It also revealed interesting details of the growth and behavior of the fungi within the skin. It could be shown how the filaments grew through the cell, how they discharged their spores and degenerated.

Mosaic fungi were found in 44 of the 134 persons. The Parker ink method stained these the same as other fungi. No relation could be found between the incidence of fungous infection and that of mosaic fungi.

From the epidemiologic viewpoint, it was established that washing with soap has no important influence on the growth of fungi, although thorough drying of the interdigital spaces stops their growth. With marked sweating of the feet the incidence of fungi seemed to decrease.

► [In the mycology laboratory at the New York Skin and Cancer Unit, the Parker ink method was found preferable to the usual potassium hydroxide preparations only with scrapings from microsporum tinea infections.—Ed.]

Sterilization of Pathogenic Fungi by Ultraviolet. According to J. Coudert and J. Rondelet[1] (Lyon, France), sterilization of instruments used in beauty parlors, required by public

(9) Dermatologica 116: 234-243, Apr May, 1 3
(1) Ann. dermat. et syph. 85: 412-419, Jul Aug 195

health authorities fraught with difficulties in practical application. Apparatus for this purpose varies in construction and performance. The authors used a suitable ultraviolet source to test the effect on various types of yeast or fungi often found on the skin and capable of transmission by combs and other instruments used in hairdressing. Despite the favorable circumstances of these experimental tests, resistance of fungous spores to ultraviolet was greater than that of bacteria; dermatophytes in culture *were even more* resistant.

Pathogenic fungi may be classified in three groups according to their sensitivity to ultraviolet rays: (1) destroyed by irradiation of 1-3 minutes (Candida albicans, Cryptococcus neoformans, Geotrichum candidum, Rhinocladium schenck-beurmanni); (2) sensitive spores but resistant colonies (Trichophyton schoenleini, Ctenomyces mentagrophytes, Sabouraudites canis, Sabouraudites audouini); and (3) spores very resistant to ultraviolet (Rhizopus nigricans, Aspergillus niger). In group 2, spores are sterilized by irradiation for 5 minutes, but colonies are not destroyed; they are merely retarded in growth. Irradiation of 40 minutes does not completely destroy S. canis. In group 3, spores of R. nigricans in a thin layer were sterilized in 15 minutes, whereas A. niger was the most resistant organism: spores in a thin smear were sterilized after 1 hour but those in clumps were not. In contrast, Staphylococcus aureus is sterilized in 30 seconds with an ultraviolet dose of 600 ergs/sq. mm./second. The dosage applied to A. niger was 75,690 ergs/sq. mm./second.

Instruments of complex structure, such as clippers and combs, are not sterilizable by the ultraviolet apparatus currently used, particularly with regard to pathogenic fungi of the skin and hair.

In Vitro Invasion of Hair by Dermatophytes was successfully achieved by F. Raubitschek[8] (Hebrew Univ.).

METHOD.—Thoroughly washed tufts of hair from 4 healthy girls were incubated with recently isolated granular strain of Trichophyton mentagrophytes on rotary shaker for 40 days at 28 C. In 1 girl's hair dense masses of thick hyphae were found invading the substance of the hair, running parallel to its long axis. In several places the strands of hyphae formed packets of rectangular arthrospores, re-

(8) J. Invest. Dermat. 19: 164, September, 1952.

sembling the picture presented by endothrix invasion in naturally occurring tinea capitis.

No invasion of hair resembling that occurring in nature has been produced experimentally heretofore The fact that invasion occurred in only 1 of 4 hair samples raises the question whether some hair is resistant to infection in vitro and whether the mechanism is similar to the natural resistance to tinea capitis infections found clinically

12 BACTERIAL VIRUS PARASITIC AND OTHER INFECTIONS

Unusual Micrococcic Cutaneous Reactions Review of Some Basic Tenets of Micrococcic Bacteriology and Drug Resistance and Presentation of Two Cases. The problem of antibiotic resistant micrococci is ubiquitous in contemporary medicine According to *Milton Orkin*[3] (Univ of Minnesota Hosps) there are two possible mechanisms of penicillin resistance The first involves a micrococcic adaptive enzyme system in which penicillinase is produced in the presence of the specific substrate penicillin This has not been entirely confirmed in vitro but has been suggested as a working hypothesis in vivo If this were the sole mechanism of penicillin resistant micrococci it would seem feasible to withdraw penicillin temporarily from the armamentarium Later reinstatement of the drug might predicate renewed sensitivity via the process of deadaption at least until the production of new adaptive system

A second mechanism entails the selection of a few resistant mutants from a large micrococcic population as a result of destruction by antibiotic of the preponderant susceptible strains This is thought to be a likelier explanation of micrococcic penicillin resistance Selection permits survival and multiplication of the resistant strain with subsequent cross infection to others with a strain which is antibiotic resistant

Penicillin resistance entails multiple steps with gradual [illegible]lopment of resistance over months to years In contrast

(3) A.M A. Arch Dermat. 78 378 385 Sept 1958

organ ms usually possess more genetic variability Therefore if the mechanism of selection is accepted, the temporary remo al of a given antibiotic might permit renewed sens tivity on later rein tatement via the proces of genetic variability

Production of disease by m crococci i attributed to their ability to multiply and spread in tis ues and to their produc tion of extracellular ubstances inclu ling exotoxin leukocidin, enterotoxin, coagulase hyaluronidase staphylokinase, proteinases and lipases Culture alone i not helpful in separating micrococcic secondary nfection from colonization since micrococci frequently contam nate broken skin. The reaction of th host to infectious d sease produces the manifestations of that disease. Therefore secondary nfection is likely present if many bacteria and polymorphonuclear leu kocytes are p esent and especially when the leukocytes have phagocytized the bacteria.

The problem of antibiotic-resistant micrococci is most acute in hospital populations Micrococci are well adapted for cross- nfection in hospital for the dried organi m may remain viable and v rulent fo months or years in dust, bed di g mattresses r other fomites Micrococci may thrive for long periods in the nasal passages of hospital patient and personnel

Two cases of u usual micrococci cutaneou reactions are p esented The first patient nurse had c llulitis of the hand due to staphylococci esistant to erythromycin and sensiti e t yt tracyclin and chloramphenicol. The second patient had generalized pu tular eruption due to coagulase-positive taphylococci which wa highly sensit ve to penicillin tetra cycline and erythromycin. Treatment with penicill n and streptomycin was rapidly effecti e, but there was a recur enc 3 week later C lture then revealed staphylococci sen ti to no obioti and esistant to penicillin and tetracy h

F diagnos of n unusual micrococcic infection com plet h t ry and laboratory tudy is necessary t di tingui h between condition that may cause s m lar or identical cl n cal pattern Rapid respo se to specifi therapy indicated by ba terial antibiotic sensitivity studies is of diagnostic value. Predisposing co d tion must be sought as in monilia i Diabetes wa present in both patients described and a pan-

creatic carcinoma in the second. The cutaneous infection will probably not be permanently cured until the underlying cause is controlled or eradicated.

► [The development of antibiotic resistant strains of staphylococci has produced a major problem, especially in hospitals, and various approaches to this problem are now being tried. In addition to hygienic preventive measures, these include the development of new antibiotics and chemotherapeutic agents which are effective against the resistant strains and the enforced withholding of selected antibiotics for certain periods, after which they may be administered with the hope that the staphylococci have remained susceptible to them.—Eds.]

Bacterial Variations in Nasopharynx and Skin of Isolated Arctic Scientists are reported by Robert W. Christie[4] (Nat'l Inst. of Health). Cultures of the nasopharynx and skin of 7 members of an expedition isolated on the Greenland Icecap for 100 days were made at the beginning of the trip and just before they returned.

Staphylococcus albus was present in the nasopharynx of 6 subjects initially and in all but 1 of these at the second culturing. *Staphylococcus aureus* was present in 3 initially and in 1 of them subsequently. Diphtheroids persisted in 4 of the 5 in whom they were initially present. *Streptococcus viridans* was present in 2 subjects initially and disappeared from both. One of these subjects received tetracycline for a severe pansinusitis, but the other received no antibiotic. *Bacillus subtilis* appeared in 4 subjects in the second culturing but in only 1 initially. *Neisseria catarrhalis* disappeared from the 2 persons in whom it was present initially.

Bacillus subtilis established itself in the skin of 6 members who did not have an initial culture showing this organism. *Staphylococcus albus* was present in the skin of 7 subjects initially and 4 subsequently (1 member left the party after 5 weeks). Three persons had *Staph. aureus* on the first but not the second determination. Two others, apparently a ... m f m he ther while with the group ... m 3 and N. catarrhalis and ... from 1 each.

All but 2 members of the group washed their hands and face almost daily, sharing the same washing soap and community towel. Two members went for 100 days with almost no contact with externally applied soap and water. There were no obvious deleterious effects from not washing in the 2, though there were qualitative changes in the population

(4) New England J. Med. 258:531-535, M... 13, 1958.

of skin bacteria. Quantitat e observation were not made

From I subject a sk n culture of Staph. albus that was not sensiti to penicill n was found, but on subsequent culture a penicillin-sensitive organism was demonstrated. Infectious disease in the expedition was confined to 2 member One had pansinusiti as well as influenza, and the other had a common cold. The sinusitis (the only infection of probable bacterial origin) occurred in a man who wa hed daily

► [Not very encouraging report from the viewpoint of manufacturers of toilet soaps! The question arises What criteria were used to assess the absence of obvious deleterious effects—cultural, local or olfactory?—Eds.]

On the Nature of the Mitsuda and Kveim Reaction. R. Kooij and Th. Gerritsen[4] (Pretoria, South Africa) obtained Mitsuda reactions with suspensions of normal li er particles n patient with tuberculoid leprosy These suspen sions ga e no reaction n patient with lepromatou leprosy Th Mit uda reaction obtained with these preparations of normal tissue, containing no leprosy bacilli were s milar to those obta ned with lepromin containing leprosy bacill Bacterial filtrates f leprom n and normal tissue preparations did not ok M tsuda reaction in patients with tuberculoid leprosy Th a thors conclude that the p esence of particles essential fo evoking M tsuda reaction. The reaction is appa ently sarcoid (tuberculoid) type of foreign body reac tion a som rphic phenomenon As with lepromin, preparations of normal tissue can oke Mitsuda reactions in healthy subj t The tuberculoid or sarco d mode of reaction con dered a general predi position of certa n persons. The l ck f react ty t leprom n among infants and the gradu all dev loping esponse among growing children may be a man festation f a normal matu tion cycle. Contact with leprosy r tuberculo probably nnecessary fo development of thi reacti ty to leprom n

Beca se of th resembla ce between lep omin and K eim antigen several f the latter wer tried on patients with tuberculoid a d lepromatou lepros With K m antigen, eactio were obta ned in patient with tuberculoid leprosy and eak o bsent reactions in the lepromatou type The K eim eaction probably d ffer only quantitati ely n healthy persons d patient with sarcoidosis, leprosy and poss bly some other diseases The K eim ntigen does not ppear t contain specific ubstanc nstead, the K m

(4) Dermatologica 1 27 January 14

reaction is an expression of a sarcoid mode of reaction in certain persons. The authors consider sarcoidosis a syndrome that can be caused by many agents each giving an individual but always sarcoid type of reaction.

► [Even the originator of the Kveim reaction do not claim absolute specificity for this test. Danbolt (Acta dermat venereol. 31 184, 1957) for example, reported negative reactions only in 46 of 51 nonsarcoid patients and positive reactions only in 41 of 46 proved cases of sarcoid. He also showed that in sarcoid patients reactions were negative with Frei antigen, spleen and brain tissue, etc. Nevertheless, it has been claimed by others that positive Kveim reactions could be elicited with entirely nonspecific materials. The report by Kooij and Gerritsen claims a similar lack of specificity for the Mitsuda reaction.

It seems to us that until really specific test materials free from extraneous substances have been developed these contradictory results cannot be resolved. Whether this will ever be possible for sarcoidosis depends basically on whether sarcoidosis is a disease sui generis or is a reaction form which can be produced by various agents. In the meantime, it is well to remember that test procedures used every day for other purposes are not 100% specific. Despite the fact that the clinician may not know exactly how specific the Mitsuda and Kveim tests are, both have proved very helpful. The reason for the requirement that large particles be present in the Kveim and Mitsuda skin test materials is not known. In serologic tests also the size of the antigen particle is important that is why such technics as collodion coating are being used.—Ed.]

Immunologic Aspect of Sarcoidosis is discussed by Kenneth M. Citron[6] (London). Low tuberculin sensitivity is characteristic of sarcoidosis. This insensitivity is not an isolated finding in sarcoidosis but reflects a general deficiency of skin reactions of the delayed type. Poverty of response has been reported to several other antigens which usually elicit a delayed response including trichophytin, mumps virus and pertussis agglutinogen.

In contrast to the poverty of reactions of the delayed type skin reactions of the immediate type or histamine-release reactions are normal in sarcoidosis, and circulating antibodies develop normally in response to antigens producing immediate reactions. Thus sarcoidosis patients may have urticaria, angioneurotic edema or allergic asthma.

Experiments indicate that failure of the delayed type of immunologic response is due to deficiency of antibody in the skin. Diminished production of antibody appears to be the most likely cause of this deficiency in sarcoidosis. Recent work indicates that there is a relative deficiency rather than complete absence of tuberculin antibody in these patients. The use of tuberculin with cortisone and tuberculin in oil

(6) Brit. J. Dermat. 70 48 57, February 1958.

has revealed the presence of slight latent tubercul n sensi ti ity in man sarcoidos patients.

The K im test i of great interest in relation to the etiol ogy of sarco dosi The test material consi ts of a suspen ion of sarcoid ti ue Recently Nethercott and Strawbridge reported solation from sarcoid tissue of diammoplomelic acid and mycolic acid. These substances are known to occur in mycobact ria, but are said not to occur in normal human ti s e Th uggest that the K eim response might be a ti ue reaction t these bacterial residues of mycobacteria present n the antigen. The suggestion i trengthened by the finding that tubercle bacilli dead or alive B C G or l popolysaccharide of mycobacteria may stimulate sarcoid reac tion n sarco dosis.

I 49 pat ents w th sarcoidos the proportion with x ray o bacteriologic evidence of previous tuberculou infection was the same n the tuberculin insensitive group a in the groups sen ti by either the t berculin test or th mor sensiti v tubercul n plu cortisone test. Th s is compatible w th the v w that sarcoidosis is manifestation of tuberculous nfection i which depressed tuberculin sen tivity is a featu of th peculiar ti ue reactivity which det rmines the de elopme t of sarcoidosis Thi observation supports a causal relation between tuberculos s nd sarcoidosis. Why these pati t eact to tuberculous nfection by this unusual hist logic and immunologic response stead of by the usual caseati g t berculin-positiv eaction remains unsolved.

► (The anergy in sarcoidosis extends to various bacterial and iral allergens and is not specific for tuberculin Why should the fact that the same proportion of tuberculin insensitive and tuberculin-sensitive sarcoid patients ha evidence of previous tuberculous infection speak in favor of connection between tuberculosis and sarcoidosis The author findings, contrary to hi conclusions, bring no further evidence supporting rela tionship between these tw diseases.—Eds.)

Verrucae Plantares Symptomatology and Epidemiology ha) \ Ra mussen (Copenhagen) tates that within 1 year from Oct ber 1951 t September 195., 5,223 new patients w th plantar w rt were seen at the Finsen Institute During the sam period, ther were 2,284 new patients with extra plantar warts, and 4,609 new pat ent with plantar lesion from pres re o old patients with recurrences of planta or xtraplantar wart Among the planta wart patients, 4 4%

(7) Acta derm.-venereol vol 33, sup 1953

were preschool children 66.3% were school children and 29.3% were adults. Among the patients with extraplantar warts 11.5% were preschool children 42.9% were school children and 45.6% were adults.

Among the patients with plantar warts 90.3% had solitary and multiple scattered warts (simple type) 4.7% had mother daughter warts 6.1% grouped warts 2.3% mosaic warts and 0.7% had more than one type. Of those with simple warts 57.9% had only 1 wart 19.5% had 2, 9.1% had 3 and 13.5% had 4 or more. Although in the children both sexes showed equal numbers of plantar warts per patient, there were more per patient among adult women than among adult men. The forefoot and pulp of the big toe were more often affected in females than in males. Tenderness occurred in 76.4% of the patients 17.8% had pain at rest and 19.1% had itching. Pain increased with increasing age.

The most characteristic diagnostic signs in verruca plantaris were (1) a circumscribing hyperkeratotic ring seen on removal of superficial layers (2) a central bundle of threads running perpendicular to the surface and (3) bleeding on paring the wart down deeply. A specially superficial form of plantar wart was seen occasionally in dry plantar skin in which the hyperkeratotic ring was missing. Rare cases of keratotic growths were seen in which diagnosis could not be established by clinical examination alone. Microscopically some of these proved to be warts, others were corns and still others could not be classified. The most important lesions to be considered in differential diagnosis of plantar warts are those resulting from pressure (corns, calluses and dystrophic pressure lesion) and radiodermatiti

Incidence of plantar warts among patient at the Finsen Institute rose from 33/1 000 in 1925-27 to 425/1 000 in 1948-50. More patients come from the outer districts of Copenhagen than from the inner part. This difference was due to the school children. The newer and larger schools are situated in the outer districts and more patients come from large than small schools. Patients who did not attend school were evenly distributed throughout the city.

Frequency of bathing and of separate washing of feet and the percentage having bath facilities at home were the same for patients with and without plantar wart. However fewer plantar wart patients took baths solely at home. Among

children who had taken baths at school for less than 1 year there was a relative deficiency of plantar wart patients, but among children who had taken baths at school for 1-4 years there was a preponderance of these patients. There were more athletes among adult women with warts than without, but among the other groups there was no difference Gymnastics at school were carried out with different kinds of rubber footwear and with bare feet by the same number of persons in the groups with and without verrucae. More persons with plantar warts than without had incurred wounds of their feet within 1 year before attending the clinic. Clinically dermatophytosis of the feet was found in only 1.1% of plantar wart patients. In 7.1% of the patients, relatives in the home also had plantar warts.

Rasmussen concludes that communal baths at school are the chief source of plantar wart virus infection and are responsible for the marked increase in incidence. Wearing of rubber footwear and traumatization of the feet by doing gymnastics barefoot do not appear to lower resistance to the plantar wart virus. The increased incidence of plantar warts on the forefoot in women may be due to the increased pressure on this part of the foot resulting from wearing higher heels. This is the only auxiliary cause for the appearance of plantar warts uncovered by this study.

The most important prophylactic measure in the control of plantar warts seems to be exclusion of patients with these lesions from communal baths.

► [This 146-page monograph on plantar warts describes in detail the organization of the project and the method of collecting data. In addition there are comprehensive chapters on symptomatology and epidemiology as well as a final chapter devoted to discussion. Suggestions as to prophylaxis are presented, but therapy is not discussed. This is indeed a very comprehensive study based on many years of work and a review of considerable material. Rasmussen's conclusion that exposure to common baths at school is a major source for infection with plantar wart virus is in keeping with opinions of others. All those interested in this problem should refer to the original treatise.—Eds.]

Incidence of Verruca Plantaris (Plantar Warts) in School Population. In a survey of 2,742 intermediate and high school students in 4 schools, J. J. Gasse and R. F. Miller[5] (Jackson, Mich.) found plantar warts in 105 (3.8%). There was no difference in the attack rate between boys and girls, but the incidence of plantar warts in one school was significantly higher than in the other 3 studied.

5) Arch. Pediat. 279-284, July 1958

A careful survey of the physical plant and athletic programs at all 4 schools revealed several factors which might help to explain the higher incidence of plantar warts at one school (School A). At this school there was emphasis on an outdoor type sports program. The program was largely conducted on a blacktopped playground and many of the students wore thin soled footgear while engaged in activities on the hard surfaced play area. There was less emphasis on swimming activities at School A. The students, however, used hopelessly crowded shower and locker rooms, the floors of which were constantly wet. It was almost impossible for them to dry their feet thoroughly after showering. From the locker room to the showers the students traversed barefooted an area used by other classes on their way to and from the playground. This area became wet and muddy and could not be kept clean.

In School B and School D showering and dressing facilities were also crowded, but floor drainage was much better. The emphasis at these schools was on pool activities rather than play on hard surfaced playgrounds. At School C there was a modern pool, tile floors were well ventilated, and outdoor activities were conducted on sodded play area.

► [Obviously, opportunity for exposure to wart virus is one of three important factors which determine the incidence of verruca plantaris. The second factor is individual susceptibility to infection with the virus; clinical experience shows clearly that some persons have a much greater susceptibility than others. We also have had the impression that susceptibility to wart virus infection is greater in some families than in others. Familial susceptibility is difficult to assess, however, since there is always associated the increased opportunity for exposure among members of the family. The third important factor is trauma and pressure, which probably are among the decisive factors in determining the localization of warts.—Eds.]

ECHO 9 Virus Exanthema. James T. Prince, Joseph W. St. Geme Jr. and William E. Scherer[9] (Univ. of Minnesota) report that a generalized morbilliform rash lasting 1-3 days became epidemic in Minnesota in 1957. Some patients had fever. Commonly infection spread within families and within neighborhoods. Though rash alone was frequent, symptoms ranged from inapparent infection through skin rash with little disability, skin rash and fever, skin rash and aseptic meningitis and finally to aseptic meningitis without rash.

Each strain of virus isolated from patients was identified by appropriate neutralization tests, and acute and convalescent phase human serums were assayed for neutralizing an

(9) J.A.M.A. 167:691-696, June 7, 1958.

tibodies. The pathogen wa thu found to be a strain of the enteric cytopathogenic human orphan virus, ECHO 9 It resembled the prototype ECHO 9 in its behavior in cultures of cell from monkey kidney human amnion and the HeLa strain of human carcinoma but it was also pathogenic for ew born mice nd for tissue cultu es of human foreskin cells. In ts pathogen city for newborn mice t resembled certain European English and Canadian strains of FCHO 9

The striking change in capacity of M nnesota ECHO 9 to produce disease n mice or destroy foreskin fibrobla ts in culture apparently was cond tioned by passage of the viruses in primary monk y kidney cultures A s ngle passage in mon key kidney cell cultures could have produced such change by increa ing the concentration of v rus and/or inducing or permitting a qualitati change in irus properties.

The incidence of disease from ECHO 9 virus in Minnesota wa estimated by the Minnesota Department of Health. In tances of aseptic meni giti with or without exanthema were determ ned by canvas of 400 households randomly selected Projection from survey findings suggested that o er 200,000 cases f ECHO 9 virus infection occurred during the summ of 1957 in th Minneapol s-St. Paul area a d that a man 400,000 cases occurred in the whole stat

Th establ hment of an etiologic relation between ECHO 9 ru d xanthema should not lead clin cians to the general conclu ion that all summer rashes are caused by this irus. Su h a conclusion would not be alid even were an epidemic of ECHO 9 virus-induced disease xistent in a com m t F dence against su h a conclusion is presented by fi ding n 4 patients who had a skin rash ind stinguishabl from that caused by ECHO 9 virus, but who failed to yield laborat ry ev den e of ECHO 9 virus infection

► [Most physicians undoubtedly w uld ha difficulties differentiating this disease from others with morbilliform rash, unless they ere in region w hich ECHO 9 irus as know to be endemic or epidemic or unless the eruption ere associated with meningitis —Eds]

Erythema Infectiosum Report of Outbreak in Marshfield, Wisconsin is presented by Kenn th R. Wilcox (Wiscon State Board f Health) and Alfred S Evans (Univ of W sconsin) During 13 weeks 62 cases wer found in which rash occurred milar to that seen in erythema infectiosum Patient were aged 2 16, a d 75% wer girl The cutaneous

( ) Wisconsin M J 1 107 March, 958

eruption had two distinct patterns. Some children showed a diffuse erythema of the cheeks with a suggestion of perioral pallor All had an erythematous maculopapular rash primarily on the extremities but to some extent on the upper chest and back. The striking and highly characteristic feature was a reticular lacelike or geographic appearance This rash was transient becoming more marked if covered by a warm hand or if the patient perspired. There was questionable redness of the throat in a few patients No conjunctivitis Koplik s spots pharyngeal exudate posterior occipital adenopathy or bronchitis was noted.

The rash lasted 1 14 days The mean and mode both fell between 3 and 4 days The rash tended to disappear and reappear during the course of the disease Mild itching was noted in 13 cases Few patients had symptoms associated with the cutaneous eruption Two recurrences were noted, but observation was not long enough to include late recurrences Multiple cases in a family were frequent.

A cytopathogenic agent was obtained in human fibroblast cultures inoculated with fresh unfrozen throat washings and stool suspensions Since more fibroblasts were not immediately available it wa necessary to freeze the first passage at —20 C for over 3 weeks before a second passage could be made No cytopathogenic agent was then recovered in this second passage The cytopathogenic agent was probably labile and lost by freezing and storage

► [Erythema infectiosum apparently is not generally recognized as such by physicians when they see isolated cases This supposition is supported by the fact that persons older than 16 manifest relative immunity probably as the result of having had an undiscovered infection with erythema infectiosum during childhood or adolescence and having become immune at that time.—Eds]

Eruptive Dermatosis of Extremities Probably of Viral Origin was observed sporadically during the pa t few year in 11 children aged 9 months to 9 years by A Cro ti and F Gianotti[2] (Univ of Milan) The clinical hi tory in these patients included rhinopharyngiti or mild br nchiti not directly related to the cutaneou erupti n weakness digestive disturbance and slight fever thick eruption f lentil sized erythematous papuloid le ion copper to wine red with some purpuric suffusions especially on the legs typical distribution over exposed portion involving only arm

(2) Dermatologica 115 671-677 November 1957

and legs, neck and face (Fig 52) In the lower extremities the eruption involved the superior iliac border of the but tocks posteriorly and the inguinal groove anteriorly it reached the humeral girdle in the upper extremities and the jugular border in the neck. It showed ascendi g progression beginning in the legs. The face was the part lea t invol ed. I some cases the lesions were confluent on the knees and elbows or i previously traumatized areas. Skin folds were



Fig 52 Typical distribution of eruption on extremities (Courtesy of Crosti, A., and Gianotti F Dermatologica 15 671 677 November 1957)

th least affected. M cosas were spared, cept in a case in which ther wa an erythematous macular appearance in the buccal m cosa The eruption progressed to compl tion in a f w da and did not ncrease but persisted 30-70 days. Res l tion w accompanied by moderate lam lla desquama tion and there were no recurrences.

The cutaneo syndrome was accompan ed b superficial pol denopathy w th hard f eely m able and nonpainf l l mph nodes There was no splenomegaly the li er projected be d the costal a ch. Duri g th course of the dis ease foll cula or herpetic angina or episodes of diarrhea were observed H t logically ther wer light hyperkera tosis nd parakeratosis and d ffuse monohistiocytic infiltra t m f dermal capillaries and at th dermoep d rmal border

Cl ical and laboratory find ngs were frequent vascula fragil t w th petechial eruptio negati e skin reactions to

tuberculin streptococcus and staphylococcus moderate hypochromic anemia, slight leukocytosis or leukopenia with monocytoid histiocytic elements (2-15%) Türk cells and plasma cells. Myelograms (6 cases) showed definite increase of histiocytes analogous to those in the peripheral blood. Erythrocyte sedimentation rate antistreptolysin titer and Paul Bunnel Davidsohn reaction were normal. Cold agglutinins were absent in the serum. Electrophoretic analysis showed increase in $alpha_2$ and beta globulins and sometimes of gamma globulins.

This exanthema is definitely different in duration type and location from ordinary infantile exanthemas and in absence of lymphocytosis and splenomegaly from infectious lymphocytosis. It resembles more infectious mononucleosis which however shows more varied mobile and transient lesion less characteristically localized, as well as splenomegaly and a positive Paul Bunnel Davidsohn reaction.

► [Dermatoses in children which have failed to conform to the typical pictures of commonly known exanthems have been noted in this country. Where drug etiology and so-called toxic causes have been ruled out, pediatricians also have tended to attribute these eruptions to a viral origin.—Eds.]

Larva Currens: Distinctive Variant of Cutaneous Larva Migrans Due to Strongyloides Stercoralis. Robert P. Arthur and Walter B. Shelley[1] (Univ. of Pennsylvania) report a case.

Woman, 46, had had a pruritic erythematous urticarial lesion on the medial aspect of the left midthigh for 2 weeks. The eruption progressed from time to time in an irregular serpiginous linear fashion. Treatment with systemic streptomycin, chloramphenicol, erythromycin and penicillin was without effect. First examination showed a raised urticarial band surrounding a fine distinct erythematous central linear lesion. The central line extended a short distance ahead of the developing urticaria. It was possible to see the lesion advance after a period as short as 10 minutes. After several hours the lesion ceased moving only to resume movement the next day. Within a 5-day observation period the active end of the lesion advanced 2-11 cm. daily during a few hours out of each 24 (Fig. 53). The urticaria subsided slowly leaving a distinct brownish track.

The patient denied any travel, animal contact or previous helminthic disease. She recalled having cleaned unwashed sand-contaminated celery a short time before onset of the eruption. A diagnosis of larva migrans was made and the advancing end of the lesion was sprayed with ethyl chloride to the point of blister formation. This treatment on two occasions *did not stop the progress* of the larva. However, a single intradermal injection of [illegible]

(1) A.M.A. Arch. Dermat. 78:186-196, August 1958.

trypsin (1 ml. of concentration of 10^3 in isotonic sal ne) at the most advanced point of the lesion proved curati e.

Larva migrans due to intracutaneous S stercoralis larvae known t the parasitologist and tropical phy ician but apparently unknown to the dermatolog t. All reported cases have shown perianal topography unusual urticarial response a d extremely rapid ad ancement of the burrow



—Route of larva mapped on left medial thigh. Note rapid progress of lesion varying from [illegible] in a few hourly reports [illegible] day. Hatched areas are sites of ineffective ethyl chloride spray. Cross-hatched circle is site at which larva was stopped by injection of trypsin intradermally. Photograph was taken after urticaria had subsided, and [illegible] graphical representation of lesion. (Courtesy of Arthur R. [illegible] and [illegible] W. R. A.M.A. Arch. Dermat. 70:186-190 August, [illegible].)

Pro ed cases ha u ariabl presented evidenc of hronic intestinal trongyloidiasis

Strongyloides tercoralis is on of the true u segmented roundworms It parasiti es the intestinal tract an adult female w rm measuring bout 2 mm long nd only 50 µ wide Th a may hat h within the mucosa of the small bowel into noni fective larval stage Later inv f lariform larvae may develop the intestine o on fecally contam nated skin These larv secret proteinase, collagenase and other en zymes which permit penetration f the normal ntact epidermi and corium. They then go nto the circulation and, ia the lung back into the intest nal tract Th reinfection account for u iqu feature f l rva migra due to this

organism i e. its localization and recurrence. Strongyloidiasis is endemic in warm climates and occurs in man, but is rarely found in dogs and cats Relatively asymptomatic chronic infections occur with eosinophilia as the solitary clinical feature. The new anthelmintic, dithiazanine is effective against strongyloidiasis

The name larva currens is proposed to point up the distinctiveness of the dermatologic patterning of cutaneous strongyloidiasis Trypsin was used in treating the present infection because of the known lethal effects of all proteolytic enzymes on many nematode infections of the intestine

► [The authors propose the Latin term "larva currens, which means racing larva, to point out that this form of larva migrans is unique in its rapidity of movement as contrasted to others. In this case the diagnosis was established on the basis of clinical appearance and course of the disease It would have been interesting to see the results of stool examination which presumably would have led to demonstration of the larvae. —Eds.]

Endemic Cutaneous Leishmaniasis in France appears to be limited to the Mediterranean coast with an endemic area in Languedoc and Roussillon Since 1951 P Rimbaud, J A Rioux and F Duntze[4] (Montpellier) studied 8 cases in which the diagnosis was confirmed and 2 others seen after a therapeutic test The actual number of cases is probably greater than reported since some lesions seen by general practitioners probably escape detection The oriental sore" in this region is atypical it develops slowly without subjective sign and displays a tendency to spontaneous cure after many months Even when the diagnosis is suspected search for the parasite is sometimes negative in old lesions

Oriental sore is caused by a protozoa of herpetomonas type the Leishmania tropica related to but different from L. donovani which is responsible for kala-azar Epidemiologically it is assumed that the disease affects animals primarily but produces an occasional isolated case in humans Wild fowl and dog are suspected Localization of lesions on exposed parts indicates inoculation by a stinging insect Phlebotomus papatasii a Mediterranean species is the principal vector

The lesions are situated exclusively on the face particularly on the protruding portion of the cheek They may be observed at any age (2-80 years in this series) The incubation period is difficult to estimate since usually the time of the in

(4) Presse méd 66 897 893 May 21 1958

fecting sting is unknown. In 1 case affect ng the lower lid, it was known to be 15 days. The lesions are always solitary not painful, nonsuppurative and develop slowly Morphologically they are of four types lupoid, furunculoid, infiltrating or ocular After 1 1½ months progressive growth, the lesion becomes stabilized and remains resi tant to all nonspecific therapy recurring in situ even after radiotherapy or electrocoagulation This fixed nature of the lesion without any tendency toward extension s of prime importance in diagnosis. In some patients the lesion had been present 9 months to 3 years before it was correctly identified.

In fresh lesions a stained smear or histologic section reveals an abundance of L. tropica, but in old lesions the parasites are often difficult or imposs'ble to find. The histologic structur i that of an inflammatory granuloma in the epiderm there are papillomatosis and marked acanthosis especially at the edge of the ulcer Infiltration of th dermis is intense, with polynuclear neutrophils and eosinophils, and histiocytes. Organisms are found within the histiocytes and also free in the dermis

Antimony treatment is rapidly effective if the lesion is recent The autho generally used 2166-RP (glucantime) in an a erage dose of 0.1 cg/kg in a course of 12 intramuscular injections gi en daily or 3 times weekly If cu e is not complet second course can be given after a few weeks. No serious de ffect ha e been observed. In 1 patient local injections of em tin cured the lesion n 1 month.

Cutaneous Amebiasis Clinical and Anatomicopathologic Study Skin condition caused by Endamoeba histolytica may be classified into true cutaneous amebiasis in wh ch the protozoon present, and dermatoses (amebides) in which the protozoon ne er found in the skin lesion True cutaneou amebiasis ra e C Pozzo and R. Rabotti (Uni of Milan) describe the first case reported so far in Italy

Man, 55, had history of exudati pleuri y and untreated dysenteric diarrhea At age 22, lesions of papillomatous type in the anal and perianal region were treated surgically w thout much success. At 28, lesion of the same type appeared on the prepuce and at 30 besides recurrence of the same lesions in the anus, perianal area and prepuce the first lesions of papillomatous-granulomatous type appeared on the anterior portion of the hard palate. On examination egetau and granulomatous lesions were found on the face 5th toe nal and perianal regions and prepuce (Fig 54) With irradiation and an-

Giorn ital dermat ... sif 99 ... 74, Mar Apr 1958.

organism i e. its localization and recurrence. Strongyloidiasis is endemic in warm climates and occurs in man but is rarely found in dogs and cats Relatively asymptomatic chronic infections occur with eosinophilia as the solitary clinical feature The new anthelmintic, dithiazanine, is effective against strongyloidiasis

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(4) Presse méd 66 897 898, M y 21 1958

Man, 35 had had highly pruritic papular dermatitis for 2 months. The eruption consisted of groups of papules and vesiculopapules, 1 5 mm. in diameter occurring mostly on the left arm and forearm (Fig 55) left thigh and leg and left side of the trunk. The lesion resembled insect bites. The patient had cat which had started t scratch it self and began to lose hair about 2 months previously H also noted that papules ppeared on his skin soon after contact with the cat.

Examination of the cat revealed the presence of a mite which was identified as Cheyletiella parasitivorax. An itching papule appeared on the patient s skin about ½ hour after a mite wa placed on hi fore

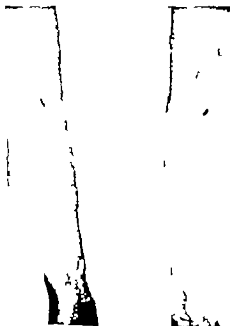


Fig Eruption on left forearm Courtesy of Parlo, V and Marcus, A Acta dermat venereol 37 37 Jan 1957

arm E en after prolonged contact th the cat, the patient wife showed no mite bites. After treatment with DDT powder the cat stopped scratching and the patient dermatitis cleared.

Cheyletiella parasitivorax ha been found chi fly n the f f rabbit d hares but occa ionally also o cats and dog In some instances the mite causes no irritation of the ki f the host, in others it hing occurs as n th s case

* [The failure of some persons, including the patient ife to react to this mite is noteworthy Probably those ho react ha undergone allergic sensitization to the mite or its products —Eds]

tibiotic and hormonal treatment, the lesions of the face regressed slightly. Later they progressively extended to the central regions of the face. The dermatosis then became infiltrative, destructive and phagedenic and resulted in massive cutaneous, muscular and bony destruction. The patient general condition deteriorated, and a severe anergy was thought to be responsible for the spreading of the condition and its destructive phagedenic aspects.

Reactions to tests for syphilis, negative until the patient was 30, became suddenly strongly positive with all antigens and at first were not modified by intensive therapy. Sedimentation rate was high. Biologic tests on various animals, cutaneous and intradermal injections with numerous antigen and cultures on various mediums always gave negative results. In the terminal stage E. histolytica was found microscopically in biopsy specimens from the ulcerations. Histo-



Fig. 54.—Localization of ... and granulomatous lesions ... objects findings on admission to clinic (Curtis ... of Porto, ... and Rabotti, R. Gior. ital. derma ... 99:40 74 Mar Apr 1958.)

logic study (biopsy specimen of granulomatous ... areas always showed ... tive epithelial ulcerations, small ulcerations and marked inflammation. In the fibrinous necrotic matter of the ulcerations were epithelial fragments, infiltrates, mainly leukocytes, and inflammatory element. On emetine treatment the skin lesion improved but the general condition was extremely po... and the patient died.

It is suggested that the massive symmetrical destruction of facial skin, muscles and bone was due not only to the lytic action of E. histolytica but also to a trophic disturbance, very likely of nerve origin.

► [Patients complaining of or giving history of dysentery who present anal or perianal ulcerations or papillomatous or granulomatous lesions should be investigated for amebiasis.—Ed.]

Dermatitis Caused by Mites (Cheyletiella Parasitivorax) Living on Cats. Veikko Ursila and Ali Murma[4] (Univ. of Helsinki) report a case

(4) Acta dermat.-venereol. 37:37-351, ...

Man, 35 had had highly pruritic papular dermatitis for months. The eruption consisted of groups of papules and vesicopapules, 1 5 mm. in diameter occurring mostly on the left arm and forearm (Fig 55) left thigh and leg and left side of the trunk. The lesions resembled insect bites. The patient had a cat which had started to scratch itself and began to lose hair about 2 months previously. He also noted that papules appeared on his skin soon after contact with the cat.

Examination of the cat revealed the presence of a mite which was identified as Cheyletiella parasitivorax. An itching papule appeared on the patient's skin about ½ hour after mite was placed on his fore

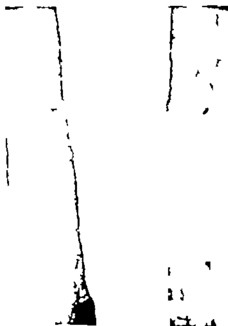


Fig. 55. Eruption on left forearm (Courtesy of Perla, V. and Marmon, A. Acta dermat venereol 37 37 30 1957)

arm Even after prolonged contact with the cat, the patient's wife showed no mite bites. After treatment with DDT powder the cat stopped scratching and the patient's dermatitis cleared.

Cheyletiella parasitivorax has been found in the fur of rabbits and hares but occasionally also on cats and dogs In some instances the mite causes no irritation of the skin of the host, in others itching occurs as in this case

► [The failure of some persons, including the patient's wife, to react to this mite is noteworthy Probably those who react have undergone allergic sensitization to the mite or its products —Eds]

Pigeons Acting as Vector in Acariasis Caused by Dermanyssus Gallinae (DeGeer 1778) Gerard A DeOreo[7] (Cleveland) reports 14 cases of acariasis due to D gallinae (the chicken mite) with the pigeon acting as the source of the mites In 7 patients the offending mites were found and identified as D gallinae. In the other 7 pigeons were found in each instance nesting on or within a few feet of their homes however mites were not available for identification. The mites hide during the day and feed at night.

The commonest lesion seen in these patients was an erythematous papule usually about 1 cm in diameter and resembling a mosquito bite. A tiny hemorrhagic punctum could be detected in the center of the lesion The dermatitis was characterized by clustering of 3-6 single papules Occasionally vesicles were observed less often large urticarial plaques. Papular urticaria was seen in 2 children. Secondary pyoderma occurred in 2 patients Chronic irritation produced localized neurodermatitis in 2 others An infant had a generalized toxicoderma associated with mild constitutional reactions

Successful treatment depends on recognition that the common pigeon may be the source of avian mites in patients with bites resulting from arthropods Increased interest in mites as vectors of disease in man and domesticated animals has led to the development of many potent acaricides including chlorophenothane (DDT) chlordane and lindane An emulsion containing benzoate benzocaine and DDT is a useful repellent when applied to the skin

► [A probably much overlooked dermatitis Pigeons on roofs and window ledges are indeed common in New York The modern air conditioner which extends outward from the window frequently may well provide space between it and the window ledge for nesting pigeons Dermanyssus gallinae might invade the air conditioner and literally be blown into the room together with the "fresh air."—Ed]

Pyoderma Gangrenosum Associated with Hypogamma globulinemia Report of Two Cases is presented by David Bloom Dorothy Fisher and Marvin Dannenberg[8] (New [illegible] S[illegible] [illegible] Hosp)

[illegible] Exacerba[illegible]
[illegible] despite [illegible]
[illegible] acetic
[illegible] peroxide
and local treatment with strep[illegible] [illegible]
and electrodesiccation Recurrences of pyoderma [illegible] ceased [illegible]

(7) A.M.A. Arch. Dermat 77 422-425 April, 1958
(8) Ibid., pp. 412 421

tirel after injections f gamma globulin. Three series of 4 injections each, given every other day with each series totaling 40 cc., were gi en within 7 months. One month later 8 weekly injections totaling 40 cc. ere gi en.

CASE 2.—Man, 55, had been observed for several years and had responded temporarily on several occasions to antibiotics and general supportive therapy. After large doses of gamma globulin, blood transfusions and upporti and steroid therapy the progres i e and extensive ulcerations epithel zed and there w almost complet cessation of recurrence of the eruption. Initially gamma globulin w used in doses of 5 cc. twice a week, but when the dose w finally increased to 20 cc. twice week improvement wa more rapid.

In contrast t agammaglobulinemia, which is frequently sociated with absen of circulating ant bodies nd w th a l w titer or complete absence of isohemagglutinins, in hypogammaglobulinemia the immunologic mechan m are not completely paral zed, though there may be a reduction of antibod es and a low titer f isohemagglut nins. Thu the second patient reacted to tuberculin and smallpox vacc ne and the isohemaggl tinin were with n normal lim ts, though of low titer. The bone marrow wh ch in agammaglobul emia hows absen e of plasma cells, was normal.

Ulcerati e col t s or a y other visceral di turbance f present, is not lways th cause of pyoderma gangrenosum. It i assumed that both the isceral and cutaneou in olvement are due to weakened mmunologic esistan e of the host. The fi d ng of hypogammaglobuli emia associated with pyoderma gangrenos m may be a forward step toward elucidation of the low esistance of the host in pyoderma gangrenosum. Futu e estigatio w ll possibly lead to discovery of ther mmune mechan ms and the r defects n this d sease thus explaining more fully the tat of weakened es stance of th host, sinc hypogammaglobulinemia appear to be ly one f many factor wh ch determin the low res tance.

Steroid may be of value n controlling ulceration in pyoderma gangrenosum. Therefore, thei adm n stration should be tried in connection with other upportive therapy and antibiotics. The explanation gi en by Wright and Greco fo the beneficial effect of steroid in some cases of pyoderma gangrenos m, viz. that some harmful, violent, antibody reaction may be suppressed by these hormones seems logical.

► [W had the opportunity to observe the astonishing improvement and healing of the deep ulcerations in the authors' Case 2. The optimal treatment for cases of pyoderma gangrenosum at present pparently is combined corticosteroids and gamma globulin.—Eds.]

Pyoderma Gangrenosum with Unusual Syndrome of Ulcers, Vesicles and Arthritis. Samuel Ayres Jr and Samuel Ayres III[9] (Los Angeles) report 4 cases. Each patient had typical chronic recurrent spreading ulcers with raised purplish borders and erythematous halos. All had fairly severe chronic arthritis and in 3 it was of the rheumatoid type. No patient had evidence of ulcerative colitis or other debilitating disease. Two patients had a superficial cutaneous eruption resembling dermatitis herpetiformis. The eruption was symmetrical, pruritic and consisted of crops of vesicles



Fig 56.—Vesicular lesions and scars on buttock and thigh (Courtesy of Ayres, S., Jr and Ayres, S. III A M A Arch Dermat 77 269-280 March, 1958)

(Fig 56) vesicopustules, papules and crusts. A third patient had had crops of blood blisters. All patients were benefited but not cured by sulfapyridine or salicylazosulfapyridine. Benefit included response of vesicular lesions as well as ulcers and in 1 case there was also improvement in the arthritis.

Vesicular eruptions resembling *dermatitis herpetiformis* in association with pyoderma gangrenosum have been previously reported with control of both the ulcerative and vesicular lesions with sulfapyridine. Arthritis associated with ulcers has been mentioned by a number of authors but has never been emphasized except in a report by Perry and Brunsting in which arthritis occurred in slightly more than half of 19 cases.

(9) A.M.A. Arch. Dermat. 77 269-280 March, 1958.

It is curious that an eruption which looks so much like dermatitis herpetiformis should also respond to the one drug which uniquely benefits that disease at the same time sharing the benefit with the ulcerative lesions This has caused the authors to wonder whether the ulcerative lesions might represent an aberrant form of dermatitis herpetiformis.

The concept of pyoderma gangrenosum has been broadened to include symptomatology and therapeutic responses not originally contemplated in earlier reports. The essential cause or causes remain unknown. The authors agree that the disease is not primarily a local infection and does not necessarily depend on an underlying debilitating condition such as ulcerative colitis or other infection.

▶ [Lupus erythematosus, dermatomyositis, psoriasis, Reiter disease allergic purpura and serum sickness-type urticaria are among the dermatoses in which joint involvement may characteristically occur

Of particular interest in these cases is the development of an eruption closely resembling dermatitis herpetiformis Similar eruptions have been seen in encephalitis (personal communication from Dr H Brodhagen) and also in Hodgkin' disease after -radiation The question arises whether the mechanism producing dermatitis herpetiformis sui generis and the dermatitis herpetiformis-like eruptions accompanying other diseases is the same The fact that both syndromes respond to sulfapyridine therapy suggests that this may be so at least in some instances

How does sulfapyridine exert its favorable therapeutic effects in dermatitis herpetiformis? Is it an antibacterial, antiviral or other antimicrobial effect The fact that the eruption can be controlled in some patients for many years on such small doses as 0 5 Gm sulfapyridine daily (see Cooper, M U S. Armed Forces M J 9 910, 1958) might be considered to speak against this possibility The mode of action of the sulfonamides is made even more puzzling since certain other apparently nonantimicrobial compounds which have pyridine ring but which are not sulfonamides (e g nicotinic acid) are effective in some cases of the disease, as are some sulfonamides and sulfones which do not contain the pyridine ring

Stoughton has shown that an enzyme present in the intestinal wall of patients with ulcerative colitis is capable of producing acantholysis-type vesiculation in the skin of man Perhaps the efficacy of sulfapyridine in ulcerative colitis and in the dermatitis herpetiformis-like eruptions associated with it is based on some interference caused by the sulfonamide with the activity of this enzyme —Eds]

13 VENEREAL DISEASES OTHER THAN GONORRHEA

Should Premarital Blood Test Be Compulsory? Using syphilis morbidity in the infectious stage and syphilis mortality in infancy as two measures of the decline of syphilis during the past 2 decades, A. W Hedrich and Charlotte Sil-

verman[1] (Maryland State Dept of Health) point out that there has been a tremendous decrease in recently acquired *syphilis in the country* as a whole. The percentage decline has occurred equally in states with and without a compulsory premarital blood test law This suggests that the compulsory *premarital blood test laws exert little influence* on syphilis mortality and morbidity Other factors such as prenatal blood testing improved case finding and particularly penicillin treatment have more likely been responsible for the rapid decline in syphilis. Premarital blood testing reveals so few infectious cases of syphilis as to make it an unproductive as well as an enormously expensive method of case finding Added to these deficiencies is the increasing problem of false positive reactions in blood tests which will become even more serious as syphilis declines further Compulsory premarital *blood test laws* may create more penalties than benefits for the population and can no longer be justified.

► [We share the opinion of Hedrich and Silverman and others that compulsory premarital blood testing should be abandoned. The article points out that the cost of finding 1 infectious case of syphilis by this method now probably exceeds $25 000.—Eds.]

Epidemiology of Syphilis Causal Factors in Present Tendency Toward Its Recrudescence evident since 1955 are discussed by A Touraine[2] (Paris) Although until 1954 there was a considerable decrease in the incidence of syphilis this was not so great as indicated by the statistics usually cited, which give reductions of 66-92% depending on the country These figures compare the period of 1943-47 with that of 1952 55 i e the base used was a period of increased incidence owing to World War II To be more exact comparison should be made with the period of 1930-39 during which syphilis was considerably more stable and exposed to normal social conditions When this period is used as a base for comparison the decrease in syphilis is not over 26-80% The recent decrease in incidence of syphilis may be no more than one of the many fluctuations exhibited by this pandemic every 8-15 years. Serologic investigations show that acquired latent and congenital syphilis have decreased less than clinical reports would indicate Syphilis appears definitely to be increasing since 1955 to judge by the growing number of primary and secondary cases registered by sev

(1) Am J Pub. Health 48 125-132, February 19 8
(2) Presse méd. 65 1851 1854 Nov 16, 195

eral countries despite their vigorous antivenereal disease programs.

Factors capable of causing a recrudescence of syphilis are always present. Some are inherent in the population of a given country. Of these, some causal factors are individual and relatively less important, such as negligence in hygiene and physicians who fail to recognize syphilis or fail to participate in the campaign against venereal disease. General factors are more important. Some of these are tied up with economic conditions. In periods of prosperity prostitution and venereal disease flourish. In periods of depression, prostitution and syphilis decrease. Great movements of population always favor outbreaks of syphilis as illustrated by wars, universal expositions, etc.

Certain social classes are more affected than others and for this reason more dangerous for the whole population, e.g. prisoners, foreign travelers and clandestine prostitutes. General welfare demands an attempt to reduce these factors of pollution and most so-called civilized countries have developed antivenereal disease campaigns which should be maintained and strengthened.

Important endemic areas of syphilis persist in various parts of the world and affect a fourth to over half of certain groups. These areas have been studied and mapped and collective measures have been instituted. These studies have shown that Bosnia, Madras, South Africa and Tahiti are among the regions where syphilis has not decreased. Each country should protect its frontiers by rigid control of immigration from these dangerous endemic areas.

Prevalence of Venereal Disease in Prostitutes. Results of examination of women arrested on charges of prostitution in New York City during 1950-56 were analyzed by Theodore Rosenthal and Jules Vandow[3] (New York City Dept. of Health) and compared with similar data obtained during 1936-46. The number of prostitutes arrested annually decreased 49% from 1940 to 1952, but increased 26% from 1952 to 1956. During the past 10 years the number of white women arrested declined 73.2% but the number of nonwhite women declined only 24.6%. Of the white women arrested, one-fifth were aged 20-25 and another one-fifth 25-30. Of the nonwhite

(3) Brit. J. Ven. Dis. 34:94-99 June, 1958.

women arrested one third were aged 20-25 and one-third 25-30

There was a marked decrease in the number of women found to be infected with gonorrhea only 5.2% in 1956 compared with 23.6% in 1946 In 1936, 35.7% were infected with syphilis in 1946 21.3% were infected and in 1956, only 6.5% During 1942-46 186 cases of infectious syphilis were found (0.8% of the women examined) whereas during 1952-56, only 5 women had infectious lesions (0.04% of the women examined) The proportion of patients with latent syphilis fell from 22.7% in 1946 to 4% in 1954 However in 1955 the proportion had risen to 7.9% and in 1956 to 10.5% These increases have coincided with an increase in the number of women brought to court in the past 2 years

In New York City the prostitute plays a lesser role at present in the spread of venereal disease than the promiscuous amateur In 1943 and 1944 3,625 contacts classified as friends were examined and 54% were infected with venereal disease. Of 474 contacts classified as pick ups 52% were infected as were 55% of 58 contacts described as prostitutes but not arrested In the first 4 months of 1957 60.9% of 2,213 contacts classified as friends 44.7% of 441 contacts classified as pick ups and 51.5% of 33 contacts classified as prostitutes but not arrested were found to have venereal disease

► [The fact that prostitutes in New York City nowadays are less of venereal disease threat than amateurs represent a striking sociologic development —Eds]

House-to-House Serologic Survey with Multiphasic Screening was conducted by the New York City Health Department in the Harlem section of Manhattan over a 10-week period in 1955 According to *Theodore Rosenthal and Jules E. Vandow*[4] 23,675 persons were tested for syphilis Of 3,406 persons with positive or doubtful blood test 2,110 reported to the health department clinic and underwent a multiphasic screening procedure This included a complete physical examination repetition of the blood test genital smears for gonorrhea urine examination for sugar chest x ray and Papanicolaou smears of the cervical secretion (in women over 21)

Of the 23,675 persons tested 14,872 were nonwhite 6,701 whites and 2,102 (mostly Puerto Rican) could not readily be

(4) Pub. Health Rep. 72 969-975 November 1957

classified racially The reactivity rate to the serologic test for syphilis for the entire group was 14 4% Syphilis was found in 1,918 persons or 8.1% of those tested 40% were new cases, 911 were patients requiring further treatment and 601 had been adequately treated. Syphil s was twice as prevalent in nonwhites as n Puerto Ricans. Reactions considered as false positive apparently occurred in 31.7% of the Puerto Rican eactors— 3 times the percentage found in nonwhites.

It is estimated that 14,771 nonwhites in the Central Harlem District are in need of antisyphilitic treatment. In the two areas f East Ha lem tested, 1,235 Puerto Ricans are in need of this treatment.

Multiphasic screening f the reactors resulted in finding 18 persons with gonorrhea, 23 with previously unknown diabetes 13 women with squamous cell carcinoma of the cervix, 3 with cti e pulmonary tuberculosis and 20 with heart or l ng conditions These results confirm the value of multiphasic screening procedures in uspect neighborhoods.

[The high incidence of syphilis did not come surprise since the particular health district canvassed was know to have a particularly high syphilis rate It ould be interesting to know the total cost of such study in over 23,000 unselected subjects —Eds]

Results of Therapy of Latent and Asymptomatic Syphilis in Prison Population II Seroreversal Following Definitive Treatment as Shown by New York State Complement Fixation Test was tudied by Bernard I Kaplan James Ryan E n Thomas, John C Cutler and Oscar Jones[3] n 2,820 patient The rate of seroreversal as measured by this s ngle procedu e wa slow eaching 25% after 5 years and 50% after 11 years observation One year after the first complete evaluation tests of only 1% of patients with syphilis of 4 or more year duration had become negative as compared w th those f 14% of patient with syphilis of less than 4 years duration. At 2 years observ tio the rates were 5 9 and 23.7% respect el

The long duration f pos ti e tests in patients adequately treated for latent syphilis hows the futility of repeated courses of therapy given in hopes of achieving a further precipitous fall in the serologic test fo syphilis (STS) or of accelerating th achievement of seronegativity in persons w th persistent seropositive findi gs after an in tial adequat schedule of pen cillin r chemotherapy Fo untreated

(3) J Chron Dis 7 311 328, April, 1958.

patients who have achieved and maintained the status of latency for a period of years, therapy should be given expressly to prevent late manifestations in those who have not undergone spontaneous cure but whose status with respect to Treponema pallidum cannot be determined by any antemortem method now known. Such therapy should be understood to have little or no effect on the achievement of seronegativity

In latent as in early syphilis the curve of the serologic fall of the given patient is often not smooth. The fluctuating nature of the STS depends on many factors in the patient and in the laboratory This must be recognized for what it is and a single increase in titer should not be interpreted as an indication for further treatment on the assumption that a serologic relapse is occurring

Diagnostic Significance of Herxheimer's Reaction in Primary Preserologic Syphilis was studied by Frances Albertazzi[4] (Univ of Turin) Sodium penicillin 100 000 units, was given intramuscularly to 17 hospitalized patients with untreated primary syphilis in the preserologic stage after which the temperature curve was studied The antibiotic caused intense general reactions (headache myalgia, malaise) in all patients after 4-5 hours and the temperature rose to 100 4-102.2 F in 9 patients and to about 104 F in the others after 7-8 hours. All symptoms subsided within 12 14 hours Although the serologic tests remained negative while the temperature was high they became positive after varying intervals of time (in 6 patients 48 hours after injection)

Appearance of the positive reaction is ascribed to the powerful antispirochetal action of penicillin, which on liberating massive doses of antigen stimulates the production of reagins capable of conditioning a positive serologic reaction.

Because relatively small doses of penicillin caused a marked febrile reaction in all these patients it is concluded that when for various reasons a clinical diagnosis of primary syphilis in the preserologic stage cannot be established bacteriologically Herxheimer's reaction caused by injection of a small dose of penicillin can be a valuable diagnostic tool. The definitive diagnosis can be confirmed as the clinical and serologic findings become evident.

(4) Minerva dermat. 33:245-247 July 1958.

Effective Simplified Serologic Test for Syphilis Employing Reiter Protein. George H. Kostant and Louise C. Kelcec[7] (New York Uni Post-Grad. Med. School and Skin and Cancer Unit) evaluated the Reiter protein complement fixation test (RPCF) using the soluble thermolabile protein fraction of cultured Reiter treponemes as antigen, in 61 patients with treated and untreated early syphilis 95 with late and late latent syphilis 21 with central nervous system syphilis and 17 with congen tal syphilis. The specificity of the procedure was also evaluated in 41 normal seronegative patients and 167 nonsyphilitic biologic false pos tive reactors. Comparison of the sensitivity and specificity of the RPCF with the Treponema pallidum complement fixation test (TPCF) was the prime objective of the evaluation since the technics of the two procedures are identical in that the one-fifth volume Kolmer Wassermann technic is used in each.

Results of the study indicate that the RPCF compares favorably n sensitiv ty with the TPCF using a desoxycholate aqueous extract of th virulent Nichols-strain treponeme as antigen. The specificity of the RPCF in this study was 100% as there was no reacti ty with the serums of normal patients or biologi false pos tive reactors. The RPCF has the advantage of inexpensiveness f the antigen as well as simplicity of performance and suitability for mass testing

► [This and previous reports indicate that the Reiter protein complement fixation test is highly specific and sufficiently inexpensive and technically simple as to be practical. It is interesting to reflect that hat started with Robert Nelson outstanding contributions to the serologic study of syphilis, such as the treponema immobilization test and the immune adherence phenomenon, has brought the development of highly specific test which utilizes conventional serologic technic and an antigen derived from strain of cultured spirochetes hich has been ailable for many years! —Eds.]

A Lipopolysaccharide Antigen of Reiter's Treponema was demonstrated and ts properties were studied by G D Alessandro nd C Del Carpio[8] (Univ of Palermo) The process of prepa ation was based on treatment of a cultured Reiter stra f Treponema pall dum with sodium desoxycholate (Portnoy and Magnuson) subsequent extraction with tri hloracetic acid and precipitation of the antigen with ethyl alcohol. The lyophil ed antigen dissolved in 0.85% sodium hloride (1 mg /ml) esulted in an opalescent solution and had in vitro and n vivo antigenic power

(7) A.M.A. Arch. Dermat. 78 11, 13 August, 1958
(8) Minerva dermat. 33 11-215, May 1958.

The lipopolysaccharide antigen elicits in animals the formation of antibodies immune serums of rabbits repeatedly inoculated with lipopolysaccharide reacted to the homologous antigen Serums of rabbits infected with virulent T pallidum (Nichols strain) reacted to cardiolipin Reiter protein antigen and Reiter lipopolysaccharide antigen Of 25 serums of rabbits infected with the same strain all reacted to complement fixation with lipopolysaccharide antigen The chemotherapy of syphilitic rabbits besides causing disappearance of antibodies to cardiolipin and treponeme protein antigen leads to a negative reaction to the lipopolysaccharide antigen.

Antipolysaccharide serum showed a marked positivity to the homologous antigen but did not react to cardiolipin or Reiter protein antigen This antiserum was positive however with suspension of treponemes. Negative reaction to the lipopolysaccharide of Salmonella typhi conformed to the specificities of bacterial lipopolysaccharide antigens. The lipopolysaccharide antigen was tested with various immune serums obtained from rabbits and guinea pigs by inoculation of Reiter protein antigen The results were negative or insignificantly positive and the authors infer that in the preparation of Reiter protein antigen the lipopolysaccharide antigen is not present or if present in small traces only

Of 85 serums from patients with latent syphilis positive to standard tests and to the Nelson and Mayer immobilization test 76 were positive to complement fixation with the new antigen The serum of 10 patients with latent syphilis positive to the immobilization reaction and negative to complement fixation with cardiolipin and Reiter protein antigen did not react to the new antigen The serum of 6 patients without a history of syphilis negative to the immobilization test very likely biologic false positive gave positive reaction to complement fixation with cardiolipin and to Kahn s test but negative to complement fixation with Reiter protein antigen and with the new antigen

Tentative studies are in progress to isolate the lipopolysaccharide antigen from virulent T pallidum

Common Contagious Genitourinary Diseases with Reference to Ito-Reenstierna and Frei Tests. In about 200 patients with penile lesions seen aboard a troop hip in the Pacific zone Donald E. Tyler[9] (Rochester Minn) found only 15

(9) Brit. J Ven. Dis. 33 228 241 December 1957

w th lesions or buboes characteristic of chancroid and posi tive reactions to the Ito-Reenstierna test. Of 14? men with penile lesions that did not appear to be chancro d, 7 had reac tions to the test. Only 5 of more than 100 who had had penile lesions in the past (nearly all diagnosed as chancroid) had reactions. Thus, it appears that the incidence of chancroid with that of other penile lesion in the Pacific zone is prob- bly less than 15% In the patients with pen le lesions only 1 Frei reaction was observed and only a few had primary syphilitic lesions.

Most of the non yphil tic pen le lesions associated with negati e Frei and Ito-Reenstierna tests had been diagnosed by other phy icians as chancroid, but most more nearly re- sembled herpes genitalis. Herpetiform les ons are apparently not specific for herpes simplex, and studies of smears from many lesions suggested the possib lity of other etiologic fa tors.

The commonly seen simple penile lesions and the urethri- tides affect the Ito-Reenstierna test similarly namely a light effect s milar in degree to the nonspecific effects pro- duced by immu ization procedures against smallpox, cholera and typhus Other imilarities in these two diseases are the cubation periods, appearance of the ulcers, recurrent na ture purported causes f recurrence not uncommon coexist ence and association of chronic external penile lesions a well as hronic urethritis w th Reiter s syndrome.

Herpetif rm penile lesio s and urethral discharges in young men are pparently caused by organisms transmitted by sexual ntercourse Because the etiologic agents of *so few* appa ently nfection lesions of the mucous membranes have been determined or ca readily be isolated a new concept of venereal disease is proposed, based on the contagious nature of gen tourinary fections rathe than on whether or not i tercourse is the usual mod of transm ssion of a particular organism Beca se the term venereal disease is emotion- lly associated with moral alues it is uggested that knowl- edge of these diseases w ll be facilitated by deleting th e term from the medical literature and substituting the term con tagious genitourinary diseases for all transmiss ble genito- urinary diseases, whether r not the specifi cause is known

► [It is, of course, possible that other micro-organisms could cause le sions hich look like herpes simplex However if the author ants to show that in his case material the penile lesions were due to other micro-

organisms he either has to demonstrate such organisms or at least show that herpes simplex virus was absent.—Eds]

Group Specificity of Psittacosis Lymphogranuloma Venereum Group Skin Test Antigens in Lymphogranuloma Venereum Patients. Maurice R Hilleman Aston B Greaves and Jacqueline H Werner[1] (Washington D C) carried out skin test titrations of antigens prepared from phenol treated suspensions of yolk sacs of embryonated eggs infected with lymphogranuloma venereum meningopneumonitis ornithosis feline pneumonitis psittacosis and mouse pneumonitis in serologically proved lymphogranuloma venereum patient For assay 0 1 ml lymphogranuloma venereum antigen containing 0 1 0.2 0 4 0.8, 1 6 or 3.2 complement fixing antigen units was injected intradermally on the volar surface of one arm and the same number of units of a heterologous antigen were injected intradermally in the other arm of a patient. Normal control antigen in greater concentration of yolk sac than that of the viral antigens was also given

The various psittacosis lymphogranuloma venereum group antigens tested were remarkably group specific in that all six induced a positive reaction in the lymphogranuloma venereum patients The amount of lymphogranuloma venereum antigen needed to give a positive test was extremely small usually 0.1 complement fixing unit or less The heterologous psittacosis and mouse pneumonitis antigens proved as active as the lymphogranuloma venereum antigen but the other antigens in most instances proved less active The antigenic differences between strains were so minor as to be of no practical consequence in attempts to obtain a species specific diagnosis in patients Instead the findings showed that any of the six antigens properly standardized may be satisfactory for diagnosis of lymphogranuloma venereum in man

It may be advantageous therefore to substitute a strain of virus nonpathogenic for man e g feline or mouse pneumonitis virus for the highly virulent lymphogranuloma venereum virus currently used for commercial production of skin test antigen This would reduce the hazard of infection of laboratory workers handling the infectious material and improve the safety of the product for the recipient

► [Obviously "false positive" skin tests for lymphogranuloma venereum can be elicited in patients who have had meningopneumonitis, ornithosis and psittacosis —Eds]

(1) J Lab. & Clin. Med. 32 53-57 July 1958.

Detection of Radiation Effects on Hair Roots of Human Scalp. Eugene J Van Scott and Richard P Reinertson[3] (Nat'l Inst. of Health) examined microscopically the roots of hairs pulled from the irradiated scalps of patients receiving epilating and subepilating doses of ionizing radiation. The types of radiation used were (1) x-rays, 2 Mev half value layer 12 cm. Cu, (2) x rays, 100 kv half value layer 0.93 mm. Al and (3) high-energy electrons 2.1 Mev

Changes in the hair root as a result of direct ionizing radiation were detected on the 4th day after exposure and were confined to anagen (growing) hairs. The earliest sign of the radiation effect was reduction in diameter of the hair bulb The matrix of the bulb when present, showed the most marked decrease. The internal root sheath of the hair bulb appeared thinner and contained dispersed pigment granules.

After the 4th postirradiation day the entire hair bulb showed progressive atrophy leaving finally only a thin strand of tissue lying below the keratogenous zone. The internal root sheath of the irradiated hair persisted and appeared thicker than normal, because of the decreased diameter of the bulb remnant which it encased.

At 2 3 weeks after exposure, hairs with tapered shafts and small keratinized bulbs were found. The keratogenous zone was absent and complete cessation of growth was apparent. Other hairs that retained the keratogenous zone and evidently produced hair shafts could be found but the shafts produced were markedly thinned.

The number of hairs showing alterations was proportional to the dose of radiation sustained by the hair roots and to the interval following irradiation X radiation and electron radiation produced the same morphologic damage in the hair roots. The dose of electron radiation delivered to the level of the hair roots was decreased in patients with increased thickness of hair overlying the scalp and in such patients fewer damaged roots were found.

Growing Hair Roots of Human Scalp and Morphologic Changes Therein following Amethopterin Therapy The

(3) J Invest. Dermat 29 36 212, September 1957

hair roots of man as in most animals cyclically pass through periods when hair is actively produced (anagen) and periods of total mitotic quiescence (telogen) Roots of hairs pulled from the human scalp may be identified as either anagen or telogen when viewed microscopically with transmitted light. An actively growing (anagen) root is characterized by a dark appearing keratogenous zone immediately distal to the hair bulb melanin pigment is usually seen in the matrix of the bulb The internal and external root sheaths may be present and intact, partially present or absent. A resting (telogen) root has no keratogenous zone and usually has no melanin pigment Though the resting root has no internal or external root sheath its club-shaped keratinized tip is surrounded by an epithelial sac. Hair roots in transition from anagen to telogen (catagen) can be identified as they have *internal and external root sheaths and a keratinizing bulb.*

Eugene J Van Scott Richard P Reinertson and Robert Steinmuller[3] (Nat'l Inst of Health) examined microscopically large numbers of roots of manually extracted scalp hairs of 16 healthy adults The proportion of growing hairs was 63-96% The proportion of growing hairs of 24 patients with neoplastic diseases aged 4-89 was 24-98%

In patients given amethopterin anagen hair bulbs were found to become atrophic and temporarily produced a hair shaft markedly diminished in diameter The bulb recovered *promptly after cessation of therapy and again produced* a hair shaft of normal diameter This resulted in focal constriction of the hair shaft The morphologic changes in the roots and shafts of scalp hairs appeared in the absence of or before clinically evident spontaneous loss of hair The changes were *more severe with higher doses of amethopterin* Progressive atrophy of the hair bulb as may be seen following ionizing radiation did not occur Hair loss resulting from amethopterin occurs therefore by breaking off of the hair at a site of constriction *in the hair shaft and not by falling out at the roots.*

The presence and magnitude of the changes associated with amethopterin therapy might be useful to differentiate between toxicity due to disease and that due to drug particularly *in* patients with leukemia in whom difficulties in making this differentiation are frequently met

(3) J Invest. Dermat. 29 197 204 September 1957

► [These very careful studies by Van Scott and co-workers of hair root changes produced as result of various stimuli have demonstrated that these readily accessible structures of man can be source of useful information. This work and work currently being done by others are increasing the potential diagnostic usefulness of a few hairs which may be pulled easily from the scalp at the time of a patient office visit.—Eds.]

Mammary Gland of Guinea Pig and Its Use as Biologic Test in Dermatologic Radiation Therapy were studied in a series of experiments reported by M. Golay (Univ. of Gene-) Daily application to the nipple of a drop of Hormoestrol (50 μg./cc.) for 15 days produces mammary gland development i the mal guinea pig. These prol ferating mammary glands are extremely rich in mitoses, eas ly demonstrated by the Dustin reaction produced by injection of colchicine (50 μg./100 Gm. body weight) 9 hours before excision of the gland.

Fi days after cessation of Hormoestrol treatment, the mammary gland has already begun to regress and pyknotic mitoses are d fin tely diminished. After 15 days, almost no m toses are found, and after 45 days the gland has practically disappeared reduced merely to ts ducts.

I mammary glands developed by 15 daily applications of H rmoestrol to the nipples, an x-ray dose of 400 r at 70 50 and 43 k red ced the number of mitoses in all guinea pigs. The mammary gland is about 2.5 mm. from the surface, wher dosage at these voltages at least 75% or 300 r. If radiatio of 29 kv is used, the dose at 2.5 mm. depth i not er 50% of the urface dose, o 200 r. This dose reduced the Dustin reaction in 3 f 5 animals. A dose of 600 r (70 kv 0.5 mm Al filter) to a mammary gland stimulated by applicatio of Hormoestrol greatly reduced the number of mitoses, when mpared with th nonirradiated side in th same animal 1 day after irradiation but 15 days afterward there wa no pp eciable difference i.e x-rays apparently d d not d lay or accelerate the glandular involution. A dose of ,000 (50 k 1 mm Al) gi en bef re daily applications of Hormoestrol did not affect d velopment of the mammary gla d and m croscopically the pyknoti m toses wer the sam on the irradiated and nonirradiated sides.

I guinea p g whose mammary glands had been stimulated by 15 application of Hormoestrol petrolatum containing 20% podophyllin which was ppl ed t th left mam

(4) Dermatologica 1 8 September 1954

mary region for 4 hours produced no effect on the mammary glands

Nipple Test and Recuperation of Mitotic Capacity after Irradiation M Golay[5] (Univ of Geneva) administered x ray doses of 400 800 and 1 600 r (70 kv 5 ma 0 5 mm Al filtration 24 cm focus-skin distance) to the left nipple of male guinea pigs At varying intervals a single application of *Hormoestrol* (50 μg /cc.) was made to both nipples, with injection of colchicine 24 hours later followed in 9 hours by excision of both nipples.

With a dose of 400 r it was generally observed that after 2 days the mitotic power had not reappeared and that the Dustin reaction was greatly diminished After 5 days the mitotic capacity had reappeared and there was no appreciable *difference between the two nipples* With 800 r usually after 10 days the mitotic capacity had not reappeared, but after 15 days there was no difference between the two sides With 1 600 r the mitotic capacity had not reappeared after 15 days but was equal to that on the nonirradiated side in 20 days.

These experiments show a relation between radiation dose and time required for recuperation of mitosis i e. the time is lengthened with increased dosage In other experiments one nipple was irradiated with 2 doses of 400 r administered *1 month apart. Five days after the second irradiation* the Dustin reaction was reduced in 2 of 4 guinea pigs, suggesting that the epidermis of the irradiated nipple "remembered" the dosage of 400 r received a month earlier

Effect of X rays on Epidermal Mitoses in Human Condyloma Acuminatum *was studied by M Golay*[4] *(Univ of Geneva)* in 3 patients A dose of 400 r (70 kv 0 5 mm Al filter) was used since this is the amount which depresses the Dustin reaction in the epidermis of the nipple and mammary gland of male guinea pigs stimulated by Hormoestrol Immediately *after selected condylomas of the patient* were irradiated, petrolatum containing 20% podophyllin was applied to both irradiated and control condyloma for 4 hours. Nine hours after removal of the podophyllin ointment the irradiated and control condylomas were excised The control lesions showed *numerous* pyknotic mitoses which were absent from the irradiated lesions

(3) Dermatologica 117 17 20 September 19

(4) Ibid pp. 21-22

These findings indicate that sensitivity of human epider mal mitoses is similar to that of epithelial mitoses in the nipple and mammary gland of the guinea pig

► [An interesting and informati series of animal and human studies ith -radiation These studies once more point out that while some of the information gathered from experiments in laboratory animals may have application to man (as, for example, in the condyloma studies) it does not apply in all instances. Certainly the findings in guinea pig breast tissue are not applicable to man since instances are known in which -radiation and gamma radiation to the developing breast tissue of the human female has distinctly altered and retarded the development of the glandular elements —Eds]

Effect of Preirradiation Intraperitoneal Injection of Cysteamine upon Skin and Depilatory Reactions Produced by X-rays in Legs of Mice was investigated by C. W Wilson (Westminster Hosp London)

PROCEDURE.—The left hind legs of 11 6-week-old mice were gi en 2,000 generated at 200 kv Immediately fterward the animals were given an intraperitoneal injection of cysteamine, 3 mg./20 Gm. Then the right hind legs were rradiated similarly to the left legs. Frequent examinations were made for 28 days for any effects produced on the hai and skin of the irradiated areas.

Intraperitoneal cysteam ne injection just before local ir adiation fforded considerable protection against the skin and depilatory effects of the x-rays. Epilation was less complete and skin reactions much less severe in the legs rra diated after administration of cysteamine. The observations seem to confirm the bel ef that the primary protective action of cy teamine occurs at the ellular level

► [This and other compounds ha been shown to increase tissue toler ance to arious forms of ionizing radiation. The truly practical aspects of findings such as these have yet to be demonstrated in man While the goal is to find some means of increasing whole body tolerance to radiation, it ould be interesting to know if protective chemicals will allow normal tissue to selectively ithstand greater doses of radiation in treatment of malignant grow th —Eds]

Comparison between Visual Grading and Reflectance Measurements of Erythema Produced by Sunlight. In de ising method f skin color mea urement for verbal description or rati g scales it is desirable to contri e methods which provide parallel col mns of 2 or 3-digit number for aluation by standard tatistical methods. The photoelec tric reflecta ce meter with appropriate filters nd stand d ppears to meet th desiderat m Two general type of use f the reflectan e meter n evaluati g skin color are evident The first i expres ion of col r as tristimulus co-ord

(7) Brit. J Radiol. 3 100 301 February 959

nates for purposes of specifying skin color in terms that can be compared with ointments cosmetics prostheses and perhaps matching of recipient and donor sites in skin grafting The other general approach is to measure melanin and hemoglobin independently and thus quantitate pigmentation in the presence of erythema or evaluate the degree of erythema in patients with different basic skin colors.

Farrington Daniels Jr and J Donald Imbrie[8] (Univ of Oregon) studied 75 subjects whose backs were exposed to sunshine for 10-120 minutes A total of 1,865 sets of observations were made These observations included the visual grading of erythema and melanin pigmentation (tan) on a scale of 0-5+ and the making of reflectance measurements through red blue green and amber tristimulus filters. Comparison between the two types of observations was made, and the four glass filters were compared to narrow band interference filters.

Studies to date suggest that an interference filter with a transmission maximum at about 542 576 mμ should be used to provide a system maximally responsive to erythema. Either an interference filter with transmittance maximum between 620 and 660 mμ or a red glass filter (such as Corning glass no 2403) should be used to measure melanin independently of erythema, though some effect from oxyhemoglobin and reduced hemoglobin cannot be avoided.

► [Among the most needed of mechanical devices in dermatology is one which will read and grade in a simple way the erythema and the pigmentation produced in human skin by external agents, including various forms of radiation.—Eds]

Benzophenones. Ultraviolet Light Absorbing Agents. Benzophenones are currently used industrially to protect objects and materials that are subject to discoloration or deterioration from exposure to ultraviolet radiation John M Knox, Jere Guin and Earl G Cockerell[9] (Houston) investigated their usefulness in dermatologic vehicles as topical sun screening preparations. Benzophenones were incorporated into 95% ethanol and vanishing cream and compared in different concentrations to tannic acid para aminobenzoic acid (PABA) and currently used commercial sun screens and sun tanning products

The minimal erythema dose of ultraviolet light for white

(8) J I est. Dermat. 30 295-304, June 1958
(9) Ibid. 29 435-444 December 1957

albino rabb ts under the experimental conditions was 25-30 second This was unchanged by the appl cation of ethanol a d was 55-60 seconds when anishing cream base was applied. Tannic acid, PABA, 2,4-dihydroxybenzophenone and 3-benzoyl-4-hydroxy-6-methoxy benzenesulfonic acid were all effective ultraviolet light absorbers in 10% concentration but PABA and 3-benzoyl-4-hydroxy-6-methoxy benzenesul fon c acid were the most effective. W th the latter agent the minimal erythema dose was increased to more than an hour Concentrations of 5% of the various light-absorbing agents were less effective than 10% concentrations The best protec tion provided by any of the 24 commercial preparations tested was 3-5 minutes, and only 4 products gave such sat sfactory results

Because 2,4-dihydroxybenzophenone is insoluble in water and is almost colorless this benzophenone in an alcohol and al cone oil ehicle was chosen for clin cal studies. This for mulation appeared to provide excellent protection for photo-sensiti e persons, fishermen and sunbathers

Absorption of Antimalarial Drugs in Human Skin Spectroscopic and Chemical Analysis in Epidermis and Corium. Bertram Shaffer Milton M Cahn and Edwin J Levy[1] (U iv of Pennsyl ania) determined the concentration of some antimalarials (quinacrine, chloroquine, hydroxychloroquine d amodiaquin) in separated epidermis and corium of normal persons who had ingested these drugs. Quinacrine d h drochloride (Atabri e®) was taken i doses of 100 mg 3 times a day for a week, then 100 mg a day for 3 weeks. The dose of chloroq ine diphosphate (Aralen) wa 250 mg tw ce day f 1 week then 250 mg a day for 3 weeks. Both hydroxychloroquine lfate (Plaquenil) and amodiaquin hydrochloride (Camoquin) were taken in doses of 200 mg twice a day for week then 200 mg da ly fo 3 weeks.

All specimen how ed higher concentration of th drug the epidermis than the corium The epidermis-derm rat w about 5 1 for hloroqu ne 10 1 fo quinacrine and 15 1 r greater for hydroxychloroqui e and amodiaquin. Drug concentratio in th epidermis ranged from n average low f 19.2 µg /Gm for quinacrine to an average h gh of 31 6 µg /Gm. for modiaquin. Ep dermal concentration of antimalarials is bel eved to result la gely from the greater af

1 J Invest. Dermat 30 343, June, 1 58

finity of these agents for epidermal protein than for that of the corium although relative desiccation of the epidermis may play a partial role.

Ultraviolet absorption curves of normal human separated epidermis and corium and similar absorption curves for tissue from the volunteers who had ingested antimalarials indicated that *these drugs had no perceptible absorption effect* so far as the ultraviolet spectrum was concerned on either epidermis or corium. Superimposed absorption curves of the antimalarials indicate that their principal absorption bands occur at different points in the spectrum and that these do not correspond to the normal sunburn spectrum range. This would indicate that the antimalarials play little or no role in *modifying the normal absorption of ultraviolet light by epidermis* so far as sunburn or polymorphous light eruption is concerned. *The data further tend to substantiate the thesis* that the action of these drugs in suppressing the manifestations of polymorphous light eruption is other than that of an intraepidermal sunscreen.

► [The marked differences in the concentrations of these antimalarials in the epidermis as compared to the dermis were noted within the 4 weeks after the start of the drug. It would be interesting to learn whether the concentration of these compounds was equal throughout the epidermis or was greater in some of the cell layers than in others. If spectrophotometric examination of single or a few cells is feasible, then this method of "tagging" the epidermal cells with selected antimalarial drugs might be used as a means of studying the life cycle of epidermal cell. —Eds.]

Evaluation of Level of Properdin in Normal Adult Humans and in Certain Disease States. *Preliminary Report* is presented by Victor D. Newcomer, Earl G. McNall, Carlyn Halde, Edwin T. Wright and Thomas H. Sternberg[2] (Los Angeles). The properdin levels of apparently healthy male and female Caucasians aged 20-85 were determined to establish normal values. *A correlation between age and properdin* level was observed. About 90% of the levels of properdin in the serum of subjects aged 20-40 were 67-184 units/ml serum. In subjects aged 71-85 about 90% of the serum properdin levels were between 17 and 84 units. Subjects aged 40-60 had properdin levels averaging lower than those in the younger group and higher than those in the older group. No relation between properdin *level and sex was detected. The* concentration of properdin in a large number of Negroes was low compared to levels of Caucasians of similar ages.

(2) J. Invest. Derm. 30 221-226, May 1958.

The levels of properdin in patients with carcinomatosis, pemphigus, lupus erythematosus, herpes zoster diabetes mellitus and topic dermatitis were studied by single determinations. Some patients with herpes zoster lupus erythematosus and pemphigus had levels lower than those considered normal for the corresponding age groups. Serial determinations and study of more cases will be necessary to clarify these findings.

Significance of Redox Potentials in Physiology and Pathology of Skin. According to H Langhof[1] (Univ of Greifswald) oxygen consumption of the skin consisting of 0.8 cu. mm./hour/mg dry substance is extremely low as compared, for example, with that of the kidney tissues (25 cu mm.) Then energy metabolism occurs according to the Szent-Gyorgyi system of biologic respiration.

Many dermatoses are caused by disturbances in the ferment metabolism of the skin. The reduction ability of the germinative layer is determined mainly by the skin sulfhydryl which contains the redox systems cysteine-cystine reduced glutathione oxide, glutathione, thioglycollic acid and thiolenzymes. The ferments in the skin (hexokinase, carboxylase, succinodehydrogenase and kathepsin) are thiolferments that are activated by certain reductors and inactivated by oxidative agents. Hexokinase, which is located at the cell membrane, is closely related to the glucose assimilation of the cell. Interruption of the glucose assimilation by restraining hexokinase starts keratinization in the stratum granulosum The keratinization goes through these stages (1) stretching of colloidal dispersed cell protein to polypeptide threads (2) combining of these parallel running protein-mycelums through disulfide bridges and salt compounds between COOH and NH groups and (3) loss of swelling and shrinkage of the cell plasma dissolution of nuclei and mitochondria of the epidermis cell.

In psoriasis normal withering of the epidermal cells is restrained by abnormally high concentration of reducing agent in the upper epidermal layers. Psoriatic parakeratosis can be provoked by reducing agents and checked by oxidative agents. Oxidative agents in high doses restrain the energy metabolism of the germinative layer of the normal skin by blocking the sulfhydryl-containing ferment system. This

[1] Arch klin u exper Dermat 207 443 458, 1958

leads to a dysenzymatic hypoxidosis. Chronic arsenic poisoning with hyperkeratosis melanosis and light sensitivity is an example of the skin syndrome caused by activation of the skin redox potential The similar response of the skin after prolonged exposure to ACTH heavy metal, tar and pitch by hyperkeratosis hyperpigmentation and susceptibility to infection is interpreted as activation of the germinative layer by oxidative agents. Absence of reducing substances such as vitamins A C and B complex may have the same effect on the metabolism of the epidermis as has been noted in vitamin deficiency dermatoses such as pellagra or melanokeratosis scorbutica

Histamine Levels in Human Skin were investigated by Herbert H Johnson Jr[4] (Western Reserve Univ) All determinations were made within 24 hours in 13 cases of traumatic sudden death 12 by automobile accidents and 1 from a traumatic air embolism Earlier guinea pig experiments had shown that this interval did not alter skin levels significantly

Marked variations in human skin histamine levels were found in different regions of the body The highest levels were on the upper lip and eyelid with decreasing levels in the submental triangle scalp infraclavicular region lower abdomen and skin over the xiphoid cartilage In the scalp the average level (11 determinations) was 21 5 µg /Gm., infraclavicular region (11 determinations) 8.2 µg /Gm lower abdomen (12 determinations) 7 6 µg /Gm and over xiphoid cartilage (10 determinations) 6.6 µg /Gm Too few determination could be made in other areas to establish average levels.

On the basis of experiments with the pharmacologic method of histamine determination Halpern and associates have proposed the hypothesis that histamine exists in tissue in three forms (1) free histamine present in only minute quantities in body fluids (2) labile histamine present normally in a physiologically inactive form releasable in a few minutes by a pathologic proce such as that induced by histamine release substances and (3) combined histamine released by acid hydrolysi technics of extraction which determine both the labile and combined" histamine simultaneously

Using the microchemical method of hi tamine determina

(4) A.M.A. Arch. Dermat 76 726-730 December 1957

tion, Johnson obtained a three-fold increase in histamine levels of human abdominal skin by acid hydrolysis. These findings tend to confirm the Halpern hypothesis.

Histamine levels determined by the microchemical method in this study were comparable to pharmacologically deter mined levels eported in the literature. The latter levels also were found to increase markedly when acid hydrolysis methods were used.

Assay of Causes of Allergies by Histamine Fixation Evaluation of Results in Various Dermatoses are pre sented by J Tappeiner H Tirschek and P Wodniansky[3] (Univ of Vienna) The serum of healthy persons contains gamma globul n which in tro inactivate 20-40% hista mine They determine according to Parrot and his associates, the so-called histamine fixation capacity or histamin opexy of the serum. In allergic persons this histamine-inacti ating ability s partly or completely absent. Lack of histamine fixatio is an lmost constant characteristic of the allergi patient but not of the healthy person. Histamine fixation is independent of clinical allergic manifestations and persists after the skin changes have subsided.

The thors assayed hi tam ne fixation to clarify the posbl allergi background in various skin diseases. They confirm Parrot contention that histam ne-inactivating ability is decreased or bsent in allergic diseases.

The number f patients w th dermatoses of uncertain use was too small to reach definite conclusions concerning th allergic or nonallergic cause. An llergic background could be uspected n essential generalized pruritus and in idiopathi erythema exudativum, but not in psoriasis vulgaris

Variations in Histamine Fixing Capacity of Blood Serum in Course of Eczema in Adults may be used as a measure of the allergi terrain, nce it is absent or greatly decreased llergic persons. Edwin S di, A. Reinberg M Hincky and J Bourgeois-Sp na se[4] (Paris) exam ned 122 patients from this point of view I 75 (33 women) with atop c eczema, 57 howed no histaminopexic power and 11 showed a slight re ction thus this function was disturbed in 67 or about 90% The proportion w essentially th same in 47 patients

(3) rch klin exper Dermat 207 26 367 58
(4) Presse med 64 343 343, Feb 24, 1956.

(23 women) with contact eczema, of whom 32 showed absence of histaminopexic capacity and 7 had values decreased to 10% (normal 30%) With clinical improvement histamine fixation of serum was 15% or over in 17 of 23 patients with contact eczema and in 28 of 46 with atopic eczema. In the latter group histamine fixation increased in 30 patients, remained unchanged in 13 and decreased in 3 Of those showing improvement of contact eczema histamine fixation increased in 17 was unchanged in 5 and decreased in 1 In general the capacity for histamine fixation is increased with clinical improvement but there is no strict correlation between degree of improvement and histaminopexic increase

This correlation suggests the possibility of treatment aimed at modification of the "allergic terrain by (1) correction of metabolic disorders (spasmophilia hypothyroidism imbalance in protein lipid metabolism) (2) u e of nonspecific corticoids and (3) injections of human serum with high potency for histamine fixation This treatment produced improvement in about one third (19 of 55) of the patients in whom it was tried. In about one third of those with contact eczema recurrences were less severe and of shorter duration after serum therapy In some patients with atopic eczema, dosage of cortisone could be reduced or discontinued after treatment with histaminopexic erum this effect was most marked in 4 patients aged 60-75 Exacerbations of eczema or other allergic manifestations occurred in 3 instances (among over 100 serum injection) Similar reactions have been reported with serum injections for a thma. *Although in most cases improvement in eczema i accompanied by improvement in other allergic symptom (rhinitis asthma or urticaria) in 5 patients (2 adolescent) the asthma increased after the eczema improved*

The authors conclude that the histamine-fixing capacity of blood serum constitutes a valuable means of following the clinical course of eczema, of determining the effectivene s of therapy and of predicting recurrence Treatment with serum of high histaminopexic potency is worthy f trial particularly in patients in whom the histamin pexic capacity is decreased or absent

► [Under the circumstances, it may be difficult to ses the therapeutic effects of injection of human serums with high potency for hi tamine fixation. *In patients with atopic dermatitis it is the rul rather than the exception that the dose of corticosteroids can be reduced graduall And m*

contact dermatitis it may be impossible to be certain that recurrences are less severe and of shorter duration unless the patient is repeatedly and deliberately re-exposed to known quantities of the causal agent.—Eds.]

Pruritus and Proteolytic Enzymes. Samuel Monash and J Frederick Woessner Jr[1] (Miami) report that the proteolytic enzymes ficin, papain, pancreatin and chymotrypsin when tested by scratch testing in a concentration of 1 10 to 1 100 in buffer solution produce pruritus diminishing in intensity in the order given. The pruritogenic character of the enzymes ficin papain and pancreatin is not lost when their proteolytic activity is destroyed by heating dry at high temperatures o by boiling The pruritogenic activity of a 1 1000 concentration of lyophilized trypsin in isotonic sa line is still present e en though the dry enzyme is inacti vated by heating at 140 C. for 2 hours. Of 9 persons tested w th tracuta eous injections of unheated trypsin solution, 5 eacted w th itching lasting ½-5 minutes. Four of the 5 reactors also received injections with heated trypsin solution and all reacted with tch ng lasti g 2-4 minutes.

When Mucuna pruriens spicules were rubbed back and forth on a small area of the skin of the forearm tching was produced consistently The spicules did not lose their pru ritogenic character when heated dry at temperatures high enough to destroy thei proteolytic capacity The enzyme is ery resi tant to heat, requiring 1½ hours at 140 C. for complete inacti ation After prolonged exposure to mois tur the picules were no longer pruritogenic, though this procedure did not destroy their enzymatic ctivity

These studies fail to show a parallelism between the proteolytic a d pruritogenic activity of the enzymes and the findings do not support the theory that there is a causal relation between the two

► [The results reported by Monash and Woessner are not in agreement ith those of the original ork of Shelley and Arthur Shelley (personal communication) among other comments, tated that Monash and Woessner used such high concentrations of proteinase that the pruritus produced could be the result of nonspecific foreign protein effect rather than specific proteinase action W look forward to clarification of the differences in the findings of these investigator —Eds]

Distribution and Behavior of Cutaneous Nerves in Normal and Abnormal Skin. The ecently introduced method of vo tain ng (nerv fibers by hyaluronidase and methylene blue has pro ed dependable for identifying cutane-

1 A. M A. Arch Dermat. 78 21 217 August, 1958.

ous nerves and Koelle's histochemical staining technic has permitted visualization of deposits of acetylcholinesterase (the specific enzyme) and nonspecific cholinesterase. A. Scott[8] (St Bartholomew's Hosp London) used these technics in the study of cutaneous innervation in 31 subjects with normal skin 10 with normal skin which had been exposed to an erythema producing physical agent (ultraviolet, thorium X or grenz radiation) 10 normal subjects in whom small areas of skin had been exposed for 2 minutes to cold or heat and 10 patients with psoriasis 53 with eczema 31 with atopic dermatitis and 14 with urticaria Of the patients with urticaria 8 presented the clinical criteria ordinarily accepted for diagnosis of cholinogenic urticaria. Intradermal tests were carried out in a number of these subjects using acetyl choline (1 10 000 in saline) histamine (1 100 000) atropine (1 1000) nicotine (1 10,000) prostigmine (1 10 000) and Trafuril® cream (thurfyl nicotinate 5%) The first five materials were administered by injection in 0 1 ml doses. Trafuril® was locally applied.

It was found that sensory nerve terminations in the trunk and limbs were represented not as specialized end organs, but by fibrils ending freely in the superficial dermis, the deeper epidermis and about the hair follicles. Sensory discrimination thus depends on functional impulse variations in the nerve fiber or central neuron identification

Specific acetylcholinestera e was identified in sensory fibers but appeared to be concerned not with sensory impulse transmission but with the passage of antidromic impulses concerned in axon reflexes induced by mechanical (stroking) physical (ultraviolet rays) or chemical (histamine etc) means The presence of this enzyme appears to be related directly to the production of erythema but is not necessarily causally concerned in transmission of the nerve stimuli.

Motor autonomic nerves arborize about all the sweat glands. Normally only those nerves supplying the eccrine glands contain free acetylcholinesterase In only one state —cholinogenic urticaria—did the apocrine gland nerve supply contain this enzyme

Nerves terminating about the pilomot r apparatu did not contain acetylcholinesterase No nerve fibers en led within

(8) Brit. J Dermat. 70 1 21, January 1958

the substance of the arteriolar walls, but sensory nerve terminals were adjacent to most of them. Usually only occasional small arterioles contained specific acetylcholinesterase in the walls but in the presence of erythema this enzyme was present in all the arteriolar walls and at the ends of the adjacent sensory nerves. It appeared that the acetylcholinesterase reached the vessels by diffusion through tissue.

Nonspecific cholinesterase was present in occasional basal epidermal cells of normal skin but in all the basal cells affected by irradiation, eczematization, Trafuril® and urticaria. Psoriatic lesions were unique in that the entire epidermis contained cholinesterase deposits.

The structural form of the cutaneous nerves was not disturbed by any of the tests used or in any of the dermatoses studied.

In general the skin followed the pattern of Lewis's triple response in its reactions to test materials. This reaction consisted of a central wheal (with an injection) and a surrounding vasodilatation with visible erythema, associated with the appearance of free acetylcholinesterase in the sensory nerves and the small arterioles. The use of acetylcholine demonstrated a minor variation in that this substance had a direct effect on the vessels as well as an indirect one via the usually involved axon reflex. Mainly these tests provide a means of determining the integrity of the local axon reflex, the responsiveness of the local vasculature and the degree of permeability of the tissue tested.

Abnormal test reactions were elicited in postradiation skin eczematization and atopy. In the first two conditions the normal response was obtained only with acetylcholine. The variation from normal in the other tests appeared to be due to lack of response of small arterioles. The alterations observed in the responses in atopic dermatitis were due to the presence of tissue edema and could be prevented by use of hyaluronidase.

Though no conclusion can be reached with regard to the basic disorder in atopy, an excess of bound acetylcholine in the vessel wall may so depress synthesis of this material that arteriolar constriction results with altered vascular permeability.

► [Among] the interesting findings in this study are the altered responses in atopic dermatitis, which Scott explains on the basis of tissue edema (see also article by Davis and Lawler, this YEAR BOOK, p. 153) and the

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(8) Brit. J Dermat. 70 1 21 January 1958

Effect of Dermabrasion on Fingerprints Preliminary Report describing results in 2 cases is presented by James W Burks Jr (Tulane Univ)

Man, 33, was treated for arsenical keratoses. The volar surface of the distal phalanx of the right 5th finger, which contained a keratotic lesion, was subjected to dermabrasion. The area was planed with a Kurtin wire brush to depth at which minute herniations of yellow fat appeared. An antibiotic, absorbable gelatin powder and Telfa nonadherent strips were applied daily for 4 days, after which only Telfa gauze was used as dressing

On the 23d day after planing the crust was easily removed. The underlying skin was pink, did not have the appearance of a scar and was devoid of epidermal ridges. On examination of the area with a hand lens, the normal arrangement of whorls was seen to be replaced by minute, thin, crisscrossed and parallel linear markings similar to those on the dorsal surface of the web between the thumb and index finger

The patient observed no difference between planed and unplaned fingers insofar as appearance, motion or reactions to heat and cold were concerned, but noted more acute sensitivity to touch in the planed finger Identification experts considered the postplaning fingerprints worthless in establishing the identity of the subject.

The basic dermatoglyphic configurations of volar skin have heretofore been considered permanent and have been used as unalterable and unduplicative means of identification. This report, which describes the alteration of these patterns by dermabrasion, vitiates the principle of finger printing and therefore, has important medicolegal implications. The services of a dermatologist may be sought by the criminal in an attempt to efface fingerprints and the dermatologist must guard against the hazard of abetting such criminals.

► [The findings of Plotnick and Pinkus (see the following article) indicate that even after the epidermis has been removed the fingerprint characteristics of the individual still are discernible in double line pattern in the cutis It appears likely that the dermabrasion as performed by Burks destroyed these dermal double ridges —Eds.]

Epidermal vs. Dermal Fingerprint Experimental and Anatomic Study is reported by Harold Plotnick and Hermann Pinkus (Detroit) Fingerprint experts hold that the dermal print is of considerable practical importance in establishing the identity of bodies when the epidermis has been altered by such processes as maceration, desiccation, mummification or putrefaction. The dermal print, though finer and less clearcut than the epidermal, possesses the same ridge

(1) A.M.A. Arch. Dermat. 77:8-11, January 1958.
(2) Ibid. pp. 12-13

presence of acetylcholinesterase in the apocrine gland nerve supply only of patients with cholinogenic urticaria.—Eds.]

Effect of Inhibition of Nonspecific Cholinesterase on Perception of Tactile Sensation in Human Volar Skin was investigated by Harry J. Hurley and George B. Koelle[9] (Univ. of Pennsylvania).

METHOD.—Volar skin of the great toes was chosen as the test area because of the preponderance of specialized and nonspecialized nerve endings found there. Perception of light touch, sharp-dull discrimination, pressure and pricking pain were tested. Distilled water 0.02 cc., was pipetted onto the volar skin of one great toe within an area 1.3 cm. in diameter and 0.02 cc. undiluted diisopropyl fluorophosphate was placed on a similar area on the opposite great toe. Both areas were quickly capped with a small glass cup that was firmly taped to the surrounding skin. Both liquids were allowed to remain on the skin for 1 hour, during which time blood pressure and pulse rate were recorded every 10 minutes as a precaution against possible development of systemic intoxication. After removal of the cups the treated skin was re-examined for sensory perception. Punch biopsy specimens were taken from 2 subjects.

On removal of the glass cups, grossly visible eccrine sweat droplets were evident on the skin of the treated toes of all 4 subjects studied. The skin of the control toes showed no such secretion. After removal of the cups, no significant differences were found in sensory perception between the control and treated toes and no variation from the initial pretreatment evaluation. Histochemical studies of the volar skin treated with distilled water revealed specific cholinesterase in its normal sites, viz., in nerve fibers about the secretory tubules of the sweat glands, about the digital arteriovenous anastomoses, in red blood cells and in many free endings supplying the skin. Nonspecific cholinesterase was visualized in Meissner's tactile corpuscles. In the treated skin there was no specific or nonspecific cholinesterase.

The authors conclude that the failure to influence significantly the perception of light touch, pressure and pricking pain by local inhibition of cholinesterases by diisopropyl fluorophosphate indicates that these enzymes have little or no function in the immediate processes concerned with transmission of cutaneous sensation. Nonspecific cholinesterase of specialized cutaneous nerve endings possibly may serve a nutritional or trophic function and its depletion or prolonged inhibition (weeks to months) would produce marked alteration in cutaneous sensory perception.

(9) J. Invest. Dermat. 31:243-245, October 1958.

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(2) Ibid., pp. 12-17

details as the outer surface of the epidermis This wa upported by the authors experimental studies.

Fingerprints were made using recently amputated digits from operating rooms Subsequently the specimens were immersed in 0 25% acetic acid solution for 72 hours to produce separation of the epidermis from the dermis The macerated epidermis was gently peeled away with tissue forceps leaving a clean surface which represented the upper dermis Histologic examination of such a specimen revealed complete absence of epidermis Prints were then made of the digit from which the epidermis had been removed.

When the dermal surface wa inked the imprint consisted of a double line rather than the usual single line pattern. This was because when epidermis i removed a double set of papillae for each epidermal cr ta remains The dermal prints were identical with the epidermal ones in all details

In the preparation of the pecimen for dermal impression the digit must be heavily inked and rolled over the card with minimal pres ure If this is not done the double-row papillary ridge pattern chara teri tic of the dermal print is not obtainable

► (The role of the dermatologist may be f r eaching Thi article was written after Dr Pinkus wa consulted by police authorities concerning the anatomic ba of the differences between epidermal and dermal finger prints —Ed)

Studies on Epidermal Regeneration by Means of Strip Method. Murray C Williams and Ro te Hunter[3] *(Detroit)* investigated the relative impertance of l cf keratin cells and of cellular trauma due to dehydration f llowing the stripping procedure C vering the tripped kin with cellophane tape as an occlu ive dre ing t minimize dehydration caused a decrea ed mitotic re pon e a compared to an uncovered tripped area Theref re be ide ellular trauma, the effect of dehydration due to l t tratum c rneum appears to be one factor re p n ible f r th mit tic respon e

To study how far the mit tic unre t pread from the keratin-stripped epiderm bi p pe imen were taken from apparently normal skin at the edge of the tripped ite Skin 3-6 mm from the tripped area h ve l a i in reased mitotic count which in most cases wa nly lightly less than that of the stripped skin In all pecime i the tratum corneum appeared to be of normal thi kne nfirming the

(3) J Invest. Dermat. 29 407 413 December

clinical impression that the tratum corneum wa intact in these areas. Spread of mitoses may be due to minimal ind reet trauma to the surrounding epidermis during keratin stripping or possibly the traumatized actively mitotic cells affect the surrounding epidermal cells by direct contiguity Another possibility is that spread of m toses may be associ ated with the triple response of Lewis. After stripping of an rea too vigorously or applying an rritating substance to the surface of the stripped skin ncreased rednes and slight edema occur in thi area and a red flare appears around it.

Stud es were undertaken to demonstrate any possible change in the concentration of acid phosphatase and succinic dehydrogenase in the rap dly proliferating epidermal cells after stripping Histochemical examination re ealed no change i concentration of acid phosphatase a compared to normal controls, and no succinic dehydrogenase wa found in the epidermal cells n normal or stripped skin.

Qualitative and Quantitative Data on Melanocytes in Human Epidermis Treated with Thorium X. Renato J Sta necco (W yne Univ) observed the beha ior of melanocytes of human skin after stimulation with weak concentrations of thorium X that did not produce marked inflammatory reac tions Melanocytes reacted with increased functional ctivity but did not increase in umber when the timulation was mild M r melan n was produced and the cytoplasm became larger and polymorphic with much longer dendrites than are seen normally The number of melanocytes seemed to decrease slightly in the 2 weeks after stimulation which was pparently due to a process of elimination Some of the mel anocyt gradually mo ed up into the prickle cell layer gran lar layer and finally horny layer losing mo t of thei dendrites the process but retaining thei vital enzymatic cti ty nt l they eached the stratum corneum The den drites lost d ring migration lea e amorphon and irregula ma ses of melanin in the intercellular paces and between the kerat n heet N transformation of malpighian cells t melanocytes wa observed.

Somewhat stronger stimulation w th thorium X produced moderat crease of the number of m lanocytes per square entim ter f kin surf ce Th ncrease seemed to parallel the elongation of the t ridges and the number of melano-

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cytes per square unit of dermoepidermal junction probably remained fairly constant.

Fifteen days after the stimulus had been set the behavior of the melanocytes that did not leave the dermoepidermal junction was variable Some were small and surrounded by a vacuum-clear area having the approximate shape of the melanocyte whereas others were as large as the ones found at *7 days* This difference might signify actual shrinkage whereby an extracellular accumulation of fluid is produced. Or a process may be involved similar to that in amphibian melanophores in which the pigment granules may concentrate around the nucleus leaving the transparent cytoplasm and dendrites almost invisible. In that case, the clear area actually would be a part of the melanocyte. Depending on which of these explanations is true the increased size of the melanocytes after stimulation would be either a real enlargement, if the clear space seen later is extracellular or an apparent enlargement if the clear space is cytoplasm deprived of melanin

The demonstration of high level pigmented dendritic cells showing dopa-oxidase and tyrosinase activity after mild stimulation with thorium X seems to support the view that melanocytes are eliminated by desquamation also under normal conditions. It has been shown that the epidermis exfoliates more rapidly after small doses of thorium X This fact, together with greatly increased functional activity of the melanocytes and radiation injury possibly suffered by some of them may be the reason more cells are eliminated and at a rate so rapid they still contain melanin granules and active enzymes.

► [It may be worth repeating here that thorium X is a naturally occurring radioactive material of the thorium series which has been used therapeutically by dermatologists for over 45 years (Nagell O E and Jesner M Therap. Monatsh. 27:765 1913) It has a half life of 3.64 days and is an alpha, beta and gamma emitter Of the radiation energies produced, 92% is alpha, 4% beta and 4% gamma Experience has proved it to be a useful therapeutic agent among its actions that of excellent stimulus of pigmentation in human skin With simple precautions it is safe and easy to use. It is commercially available and may be used without authorization from the United States Atomic Energy Commission.—Eds.]

Melanocyte Distribution in Forearm Epidermis of Freckled Human Subjects was investigated by Aodán S Breathnach[5] (St. Mary's Hosp Med School London) In local

(5) J Invest. Dermat. 29:253-261 October 1957

ited areas of pigmentation (freckles) in the skin of 5 freckled subjects, significantly fewer active melanocytes/un t area could be demonstrated in dihydroxyphenylalanine (dopa) treated material than in adjacent paler areas or in corresponding epidermal areas of 5 nonfreckled subjects. The melanocytes of freckles showed characteristic signs of hy peracti ity compared with those of surrounding less highly pigmented epidermis. Supravital staining with methylene blue gave a strong impression that the difference in number of melanocytes present in freckles and surround ng epider mis is a real one in total numbers and not due to some of the cells of the freckle being in a completely nacti e (dopa negative) condition. These findings confirm conclusions of previous wo kers that a high degree of epidermal pigmenta tion depends more on the level of functional activity of the melanocytes than on the ctual numbers present in a given area

Potential frecklers are nonfreckled at birth and do not appear capable of producing freckles until ages 2-4 It is not known whether su h persons are born with localized areas of low melanocyte concentration at the sites of future freckles or whether the melanocytes are uniformly distributed as they appa ently are in the nonfreckled If the latter is the case t not known what influences operate to produce the subsequent une en distribution in numbers and pigment concentration

At the edge of a freckl there is a sharp demarcation between immediat ly adjacent area of epidermis with differ ent characteristic Whe a freckle spreads to nvolve an ad joining paler epidermal area, th latter mu t presumably take on the haracteristics of the former This must in olve reduction n the total number of cells in the paler area plus stepping up of the tyrosinase activity of the rest or the oper ation of some select influence which leads to stepping up of the ctivity of some cell and suppression of that of others, w thout at the same tim affecting the t tal number present

Observations on Tyrosinase Activity in Melanocytes of Freckled Human Epidermis re presented by Aodán S. Breathnach[8] (St M ry s Hosp Med. School London) Samples of normal human kin ea h bearing a freckle and an ea of urround ng paler skin we emo ed from the fore-

[8] J Invest Dermat 30 33 38, March, 1958

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At th edge of a freckle there is a sharp demarcation between immediately adjacent areas of epidermis with different characteristics. When a f eckle spreads to nvolve an adjoining paler epidermal area, the latter must presumably take on the haracteristics of the former This must in olve eduction in the total number of cells n the paler area plu stepping up of the tyrosinase activity of the rest o the ope ation of some selecti e influence which leads to stepp ng up of the activity of some cells and suppress on of that of others w thout at the same time affecting the total number p esent

Observations on Tyrosinase Activity in Melanocytes of F eckled Human Epidermis ar presented by Aodán S Breathnach (St. Mary's Hosp Med. School, London) Samples of normal human skin each bearing a freckle and an area of surrounding paler skin, w re removed from the fore-

( ) J Invest Dermat 30 113 118, March, 58

arm and knee Pure epidermal sheets were obtained by tryptic digestion and these were incubated with different substrate mixtures 0 05% l tyrosine at pH 6.8 with phosphate buffer similar l tyrosine solution to 50 ml of which 0 4 ml of 1% copper sulfate solution was added buffered 0 1% solutions of l tryptophan and 5 hydroxytryptophan and 0 1% dopa

A reaction developed in the melanocytes of both freckle and paler epidermis of all specimens incubated with buffered tyrosine alone. Localized variations in tyrosinase activity were observed and could be correlated with morphologic differences differences in population density of the cells concerned and with the amount of pre-formed epidermal melanin In areas where melanin was most abundant melanocytes were typically large with many branches and comparatively sparse These cells exhibited a relatively high level of individual tyrosinase activity These findings based on observations of the tyrosine reaction were identical with those achieved when dopa was used as a substrate

Differences in tyrosinase activities of the melanocytes of freckles and paler epidermis were not abolished by provision of an excess of copper in the substrate medium. This strongly suggests that the localization of individual freckles cannot be accounted for in terms of local differences in the concentration of epidermal sulfhydryls affecting availability of copper for the tyrosinase Certain natural features of freckling including its absence before age 2 3 and the sharp boundary between freckle and adjacent paler epidermis which lies within the territory of a single melanocyte tend to support this conclusion

Other factors such as morphologic differences between the melanocytes of freckles and pale epidermis and differences in population density must be considered in attempting to account for freckling If freckling were present from birth it would be tempting to suggest the existence in freckled epidermis of two genetically distinct types of melanocytes and that it is the location of representatives of these different types which determines the sites of freckles However since freckling is acquired postnatally this is unlikely No reaction was observed in melanocytes incubated with l tryptophan or 5-hydroxytryptophan therefore neither amino acid is a likely substrate in normal human melanogenesis

Histology and Cytochemistry of Human Skin XIII. Blood Supply of Hair Follicle. William Montagna and Richard A Ellis (Brown Univ.) demonstrated selectively the terminal capillaries in frozen sections of skin by use of the azo-dye technics for alkaline phosphatase. Active hair follicles have a rich plexus of capillaries around the bulb a sparser plexus in the upper part of the follicle also envelops the sebaceous glands. Straight vessels along the middle less vascularized part of the follicle connect the lower with the upper plexus. Loops of capillaries form a vascular ring around the orifice of the follicle under the epidermis. This collar is continuous with both the vascular loops of the epidermis and the network around the follicle. The dermal papilla at the base of each follicle contains a large tuft of capillaries in its center. This occupies a much larger part of the papilla than is ordinarily realized. These capillaries extend to the walls of the inner side of the follicle and are often practically in contact with the wall.

During transition from active state to quiescence the bulb atrophies and the base of the follicle moves upward in the dermis and partially out of the network that surrounds it. The dermal papilla also recedes upward and slips away from its central capillary tufts. Only part of these capillary nets seem to atrophy; most of the vascular material collapses and remains at the base of the resting follicle as a tangled bundle in contact with the free dermal papilla. Since only the lower part of the follicle degenerates when it becomes quiescent the palisade of straight vessels in the middle third [illegible] changed. Higher up around the sebaceous gland and the infundibulum the plexus also stays intact. When a quiescent follicle becomes active again the new bulb plows its way through the bundle of capillaries and grows inside it.

The capillary network from any part of the follicle and its sebaceous glands form a continuous system and each vascular bed is not. Since the pilosebaceous system functions as a unit the vascular mechanism may be responsible for this integration or at least shares the responsibility.

The follicles of vellus hair on the body skin or in the bald scalp are surrounded by very simple capillary systems. A few capillaries surround the lower part of the follicle but no vessels penetrate the dermal papilla. The enormous se

(7) J Nat. Cancer Inst. 19 45 -463 September 1957

baceous glands associated with these follicles are normally highly vascularized

Tonofibrils of Human Epidermis were studied by Arwyn Charles and F G Smiddy[4] (Leeds Univ) by electron mi



Fig 37.—Section of epidermis from extensor surface of forearm of man, aged 30. Figure shows part of outline of malpighian cell. Nucleus, n, and many mitochondria, m, are readily seen. Many prickles, p, are seen at cell periphery showing light central region, pl, flanked by electron dense lines, pd. From prickles rise tonofibrils t, ... in which tonofibrils, tf, can be distinguished. Between prickles double line representing ... walls, cw, can sometimes be seen. Reduced from × 1,500 ... series of adjacent cell ... Charles, A and Smiddy F G, J Invest Derm 29 ... November 1957

croscopy The structure of a typical prickle is shown in Figure 57 Occasionally the electron-dense lines are seen to be double and more frequently a dark line is seen to traverse the clear central region. The tonofibrils have never been seen to pass through the clear central region.

Between the prickles the walls of the adjacent cells are distinct and contiguous and when cut transversely are easily distinguishable as a double line. If dehydration is prolonged the walls tend to separate, giving rise to intercellular spaces bridged by the prickles which thus form the intercellular bridges seen in light microscopy The walls of adjacent cells are apparently fused at the prickle since cell walls have never been observed to separate at these points and the width of the clear central region of the prickle does not change

At the dermal-epidermal junction there is again seen a tonofibrillar tuft, but there is no counterbalancing tuft on the other (dermal) side. The appearance of the tonofibrillar tuft on the junction wall of the basal-layer cells can show some variation in different human material but in essence appears to be half the normal prickle which, with its two oppositely situated tufts, is the structure invariably seen between epidermal cells.

This assumption suggested that both ends of the tonofibril or tonofibrillar bundle are attached to the cell wall the point of attachment being the prickle or half prickle. The result of such an arrangement would be to link the whole of the tonofibrillar network of the epidermis into an elastic system eminently suitable for taking up the distortion strains to which the epidermis is constantly subjected. The opposite positioning, on either side of the area of adhesion, of the tonofibrillar tufts of adjacent epidermal cells becomes understandable, because this arrangement allows the advantages of the elastic system to be realized the tonofibrillar attachment at the dermal-epidermal junction however requires no counterbalancing tuft, because the adhesion between dermis and epidermis enables any strain on that point to be transferred to the dermis and to the collagen and elastin fibers found there

(57) J Invest Dermat 29 327 335 November 1957

To study the response of prickles and tonofibrils to stretching sections were cut parallel and transverse to the direction of stretching of skin fixed in a stretched state Section cut parallel to the direction of stretch were found to be cut parallel to the main orientation of the tonofibrils sections cut transversely to the direction of stretch showed transverse sections of the tonofibril bundles. Tension was found to develop at the points of anchorage of the tonofibrils on the basement membrane with consequent inward puckering of the membrane at these points

Eleidin in the stratum granulosum accounts for the whiteness of the skin according to R Lutembacher[9] (Paris) Mucous membranes which do not contain eleidin are transparent allowing the red color of hemoglobin to be seen Redness of the lips is also explained by lack of eleidin rather than by special vascularization The color of the cock comb is also due to the absence of eleidin, except for the pearly white areas in the region of the auricular orifice and on the wattles where eleidin granules may be found.

The whiteness of eleidin which like the tin foil of a mirror reflects light, is comparable to that of boric acid crystals Dermatologists recognize that in certain pathologic states, as in inflamed scars the skin may be red owing to transparency due to lack of eleidin Conversely mucosal surfaces may be abnormally white as in leukoplakia and the white streak of buccal lichen planus owing to abnormal proliferation of the granular layer and an excess of eleidin Eleidin also gives psoriasis scale their waxy appearance

Response of Human Epidermus to Application of Carcinogenic Hydrocarbons was investigated by Murray C and Williams[1] (Wayne State Univ) A 1 solution of 3 methylcholanthrene in benzene was applied to the normal epidermis of 11 volunteers No discernible change was observed clinically after the single application Microscopically a slight to moderate increase in mitoses was found during the period of study viz the first 7 days after the application

A 1% solution of 3 methylcholanthrene in benzene was applied to an area of keratin-stripped epidermis On clinical examination this area did not differ from the result for ordinary cellophane stripping painted with benzene only The

(9) Presse méd. 65 2175 Dec 25 1957
(1) J Invest Derm 30 13 20 January 1958

microscopic appearance after keratin stripp ng and paint ing with 3-m thylcholanthrene was imilar to that observed fter keratin stripping alone except that the m totic re po se m tead of be ng greater wa lghtly lower and prolo ged.

One v l nteer recei ed daily applicatio i of 9 10-dimethyl 1,2-benzanthracene i mineral oil for 7 days. One and 2 months late a si gle appl cation produced an allergic papu lovesicular response in the test site and in the areas previously painted with 9 10-dim thyl 1,2 benzanthracene Thi is n terpreted further confirmation that the immunologic ta tu of th host o e factor involved in carcinogenesis.

All subjects were f llowed 2-8 month The keratin tripped and painted area and biopsy sites healed normally

* [This appears to be the first instance in which allergic sensitization to the carcinogen 9,10-dimethyl 1,2-benzanthracene has been demonstrated. The possibility has been considered for years that llergic sensitization may play role in carcinogenesis produced by simple chemical substances Experimental investigation in animals thus far ha failed to turn up supportiv evidence (Serri, Herrmann and Kurman, Acta dermat venereol 34 248, 1954) —Eds]

Effect of Oxypsoralen on Ultraviolet Carcinogenesis in Albino Mice wa tud ed by M A O Neal and A C Griffin (Un of T xas) Swiss m ce were totally irradiated with ltraviolet lamps f 15 minutes/day The final incidence of ea tumors mice recei ing 8-methoxypsoralen (8-MP) their diet wa co derably les than that of control The extent f protection afforded by th compound ap pea ed to be proportional t t concentration in the diet up t optimal level of 0 5 Gm 8-MP/kg diet Ear tumors oc curred 32% of mice recei ing thi concentration in 39% f those receiving 1 Gm 8-MP/kg diet a l in 45% f those recei g 0 2 Gm /kg

The final tumor ncide ce mice recei ing int aperito neal njection of 0 4 mg 8-MP da ly 1 ho r b fore ultraviolet posur wa nearly 100% cr mpa ed with 68 4 in the ont d gro p A ce lerated latent period of carcinogene wa also observed. When the compound w adminis tered in the same dosag 20 hours befor rradiatio th fin l ea tumor ncidence wa i the same range a that of the contr l

There no complete explanation fo the result f these tudie The m entration f 8-MP a defin te fact r a

To study the response of prickles and tonofibrils to stretching sections were cut parallel and transverse to the direction of stretching of skin fixed in a stretched state. Section cut parallel to the direction of stretch were found to be cut parallel to the main orientation of the tonofibrils sections cut transversely to the direction of stretch showed transverse sections of the tonofibril bundles Tension was found to develop at the points of anchorage of the tonofibrils on the basement membrane with consequent inward puckering of the membrane at these points

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(9) Presse méd 65 2175 Dec 25 1957
(1) J Invest Dermat 30 13 20, January 1958

► [The results with 8-MP feedings suggest a protective effect whereas those with intraperitoneal injections indicate an increased incidence of cancer formation in mice with ultraviolet light irradiation. In any event they support the viewpoint that it is not justified at this time to recommend 8-MP tablets in man for their protective effects against the burning rays of natural sunlight.—Eds.]

Hitherto Unreported Malignant Melanomas in Syrian Hamster: Experimental Counterpart of Human Malignant Melanomas. Joseph G. Fortner and Arthur C. Allen[2] (Sloan Kettering Inst.) found primary melanotic and amelanotic melanomas in 10 (1.9%) of 523 Syrian hamsters surviving 181 days or longer. Three melanomas occurred in untreated controls, 2 in animals inoculated with bile from patients with cancer of the extrahepatic biliary tree, 2 in animals given injections of sodium desoxycholate solution, and 1 each in those given injections of ox bile, bile from patients with nonmalignant biliary tract disease and sesame oil. The tumors are considered to be of spontaneous origin since they occurred in untreated controls and in animals subjected to various experimental conditions. Of the 10 tumors, 8 occurred in males. Two were grossly melanotic and 8 amelanotic. A separate, second primary tumor was found in 5 of the 10 hamsters with malignant melanoma. Metastases were found in 9 hamsters.

Though malignant melanomas have been described in many other animal species, this is the first experiment recorded in which they were observed in the Syrian hamster. The histogenesis of the hamster melanocarcinomas appears to be identical with that of malignant melanoma in man, i.e., origin from junctional nevus. Except for one feature, the histologic appearance of the hamster melanoma corresponds well with that of human tumors. In both, there is a wide range of pleomorphism, mitotic figures and pigment content. In both the metastases may be overwhelmingly widespread. However, there is a disparity in the relation between pigment content, and degree of anaplasia and growth potential. In malignant melanomas of man there appears to be no relation between melanin content of the primary tumor and degree of anaplasia of tumor cells or their capacity to metastasize. Contrarily, the pigmented melanomas of hamsters apparently are, in mice, are far more innocuous appearing histologically than the amelanotic tumors. The

time of administration with reference to the ultraviolet exposure. Early erythema response to ultraviolet may be important in tumor formation Animals receiving 8-MP 1 hour before irradiation exhibited severe erythema of the ears face and tail with subsequent scar formation and shriveling of the ears These preliminary changes were less marked in the control groups whereas the ears of mice receiving dietary psoralen maintained a relatively normal appearance throughout the entire period of irradiation (110 days) The early damage to the ears may produce irreversible changes which with the continued stimulation of ultraviolet light, lead to neoplastic transformation

Since little is known concerning the metabolism of 8-MP it is difficult to explain adequately its mechanism of action. The protective effect afforded by oral administration of the compound might be explained by the strong absorption of this compound in ultraviolet wavelengths (3,000 and 2,500 A) The concentration of this or related compounds in the outer layers of the skin may effectively filter out the ultraviolet rays. Recently the authors observed that the shorter ultraviolet rays (2,537 A) have no effect on the action of 8-MP in the formation of pigmentation or other erythema changes In contrast severe erythema changes were found in man and animals after oral administration of 8-MP and subsequent exposure to longer ultraviolet ray The pos ibil ity exists however that with oral administration the compounds are metabolized in the intestinal tract or liver The resulting metabolites might exert a protective effect in the skin possibly by forming complexes which would act a a barrier to incident ultraviolet light

Since 8-MP absorbs strongly in the ultraviolet wavelengths, the enhancing effect produced by intraperitoneal injection might be due to an immediate concentration of this compound in the skin resulting in an increased photo en i tivity to ultraviolet light It is unlikely that a metabolite i responsible for this action since *8-MP* given in the ame dose 20 hours before ultraviolet expo ure is with ut effect ndicating that it has been metabolized to inactive pr lucts Th finding parallel the pr m te pigmenta bet veen a lmini tion in ma tration and exposure to sun.

fore sweating was replaced by concentration n the apical part of the secretory cell and around the vacuoles. Nuclei of the small dark cells increased in s ze and showed a more prominent nuclear membrane Nuclei of the large pale cell virtually lost their membrane and contained less chromatin and were les basoph lic than those in control specimens After several hours of sweating the basement membrane of the secretory coil thickened. After 1 hour of sweating there wa decrease of glycogen in the secretory cell and after 3-6 hours glycogen disappeared from most of th cell After 6 hours there was definite increase in the acti ity of esterase

The cytolog c alterations observed as the result of profuse sweating were greater than anticipated. It seem unlikely that s ch a normal function as secretion of sweat could produce frank damage to the secretory cells of the gland Pos sibly th eccrine weat gland has l mited ability to maintain profuse secretion. This is reflected in the fairly rapid change in sodium, potassium and chloride concentration of sweat and its rate of output noted as a result of acute exposure to a hot humid env ronment

Human weat glands have been divided nto two types those with mple fluid secretion the eccrine sweat glands and those i wh ch part of the cell is secreted, the apocrine gland Thi tudy show that eccrine glands also have a particulate secretion (PAS-positi e, nonglycogen material) Defi tion f the terms eccrine and apocrine on the bas s of a fundamental difference n the method of excretion may be erroneou However a change in nomenclature is not ad ocated because these terms if not taken literally retain efulness n differentiating these embryologically and anatomically d fferent types of sweat glands.

II Recovery from effects of profuse sweating was nvesti gated by Dobson and Lobitz[3] who tudied punch biopsy pecimen fr m no mal young men before and after 6 hour of profuse weating n a heat cab net At 24 hours after sweating th ll of th secr tory coil appeared larger than mmediat ly after weating although atrophy and general distortion f the secretory coil was apparent Glycogen was present in the la ge pal cell but had n t eappeared in the cell f the duct There w slight increase in the amount of PAS-positive dia tase-res tant granules within the secr

(3) J Invest Dermat 30? 1?, October 1958

capacity of amelanotic tumors in hamsters to grow and metastasize far exceeds that of the pigmented tumors.

With rare exceptions tumor implants of hamster melanoma have grown in all animals inoculated. The nearly uniform takes of implants rapid but individual growth rates of melanotic and amelanotic types and similarity to the human melanocarcinomas all result in a biologic spectrum of the melanocarcinoma which should provide a useful baseline for further investigation

Some Histochemical Observations on Human Eccrine Sweat Glands.—*III Effect of profuse sweating* was studied by Richard L. Dobson Victor Formisano Walter C Lobitz Jr and Doris Brophy[4] (Dartmouth Med School)

METHOD.—Maximal sweating was gradually induced in normal young men in a heat cabinet in which the temperature rose from 70 to about 105 F Maximum temperature was maintained 6 hour or until total failure of the sweat glands or pronounced subjective symptoms required stopping of the experiment Biopsy specimens were obtained without anesthesia by high speed rotary punch before at hourly intervals during and immediately after 6 hour of profuse sweating

Maximal generalized sweating was elicited within 30 minutes Sweating was profuse for about 4 hours then declined. At this time the subjects became restless and uncomfortable despite adequate fluid and electrolyte intake Between the 5th and 6th hours as sweating became scanty or ceased the subjects showed lassitude and malaise This was accompanied by tachycardia hyperpnea and orthostatic hypotension

Marked alterations in the structure of the eccrine sweat gland occurred After 1 hour there was a striking depletion of PAS positive nonglycogen particles in the cells of the secretory coil After 4-6 hour only the luminal border of a few secretory cells contained significant numbers of these particles The particles were excreted directly into the lumen of the secretory coil and gradually traversed the duct until they reached the surface After about 1½ hour of sweating vacuoles appeared along the basal border of the glandular cells and in the cells of the coil portion of the duct adjacent to the nuclei The secretory cells especially the large pale cells definitely decreased in size Prominent intracytoplasmic inclusions were noted in the secretory cells after 6 hour of sweating The even distribution of mitochondria noted be

(4) J Invest. Dermat. 1 14 159 September 19 8

excised after progressive time intervals. No sensitization appeared when the nodes were excised within 48 hours after the primary contact. When they were excised after 3 5 7 and 8 days, sensitization was observed in 20 50 80 and 90% of the animals, respectively To sensiti e the animal the explant must be kept in situ for at least 2 days. The time of co tact required to sensitize guinea pigs varied between 1? d 48 hours f r the explant. On the normal skin, it takes about 8-32 hours.

To examine the influence of the regional lymph nodes on the mai tenance of sensitization, the authors also sensitized animals by applying dinitrochlorobenzene to a cutaneous explant, then excised the regional lymph nodes 21 12, 11 9 and 8 days after the primary contact and tested the ani mals 1 month later Sensitization was not eliminated by th intervention i.e no animal was desensitized.

The fact that sensitization does not appear when the regional lymph nodes are excised 48 hours after th primary contact suggests the production of antibodies n the nodes E en when the nodes were excised after 7 days, sensitization did not de elop n 17% of the animal The fact that sensitization maintained when the regional lymph nodes a e excised 8-21 days aft the primary contact implies that antibodies are produced n other organs. Sensitization was maint med n 41% of the sensitized an mals the nodes of which had nly been functioni g for 6 days The authors bel ev that antibod es are produced in regional lymph nodes as well a other organs and do not believe that the role of the lymph odes only to lead the antigen to the organ sm.

Influence of Certain Neurotropic Drugs on Dinitrochlorobenzene Eczema in the Guinea Pig was studied by P de Graciansk I I ra l and J Cohen Solal[7] (Pari)

Method—Sensitization of guinea pigs w achieved by daily pplication for 12 18 days f 0 05 cc. of 0.135% solution of dinitrochlorobenzene (DNCB) After sensitization had been shown, its intensity a stimated by the quantitati e technic of Frey On reas on the flank ep lated with scissors 0 05 cc. of solutions of 0.01 0 03 0 05 0 1 0 135 0 15 0 175 and 0 2% DNCB were applied. When positiv eaction w obtained on one of the surfaces, it wa allowed to disappear (2 da) before the same quantity of the next lower concentration was applied on another site. The threshold of sensiti ity corresponded to the lowest concentration capable of provoking definite esponse in 4-48 hours. Because the initial threshold did not nec

(7) Brit J Dermat 70 340 332, October 1958

tory cells Metachromasia was either minimal or absent

At 48 hours despite great variability in cellular configuration within the secretory coil reaccumulation of glycogen and PAS-positive diastase-resistant material was relatively constant Within the duct glycogen reappeared only in the basal cells in most instances whereas within the secretory cell glycogen content was normal The amount of PAS-positive diastase resistant material within the small dark cells was greater than at 24 hours but still less than in control specimens Metachromasia was minimal or absent

At 72 hours glycogen had appeared in the luminal cell of the duct Secretory cells were less atrophic and most of the secretory coils appeared normal in configuration. Increase in the amount of PAS positive diastase-resistant material had continued and many cells showed concentration of this material along the luminal border of the cell After 5-7 days all the secretory coils and ducts examined appeared normal

Probably the most important and potentially useful aspect of this study is the observation of a difference in the recovery rate of the large pale cells and the small dark cells in the secretory coil and a difference in the time of reappearance of glycogen in the secretory coil and the duct Taking advantage of these convenient circumstances may make it possible to characterize the processes of secretion and absorption within the eccrine sweat gland

► [What happens to the sweat glands and to the systemic alteration that are a consequence of the changes in the sweat glands (produced by profuse sweating) when the experimental subjects remain in the hot environment? To what extent do they adjust How long does it take to make the adjustment? Does adjustment continue indefinitely? The question may soon be answered if studies such as these are continued —Ed]

Role of Regional Lymph Nodes in Development of Dinitrochlorobenzene Contact Eczema in Guinea Pig was studied by J R Frey and P Wenk[6] (Basel) For the primary contact with dinitrochlorobenzene an isolated skin piece or explant was used The explants were connected with the animal body either by a *pedicle containing arteries vein and* nerves or by an additional skin bridge Thus the function of the vascular nervous and lymphatic systems in the development of contact eczema could be studied individually

The animals were sensitized by applying the dinitrochlorobenzene to the explant. The regional lymph nodes were

(6) Dermatologica 116 241-259 Apr May 1958.

skin sensitization to a poison ivy allergen pentadecylcatechol (PDC) and of experimentally induced skin sensitization to 2 chemical sensitizers, 2 4-dinitrochlorobenzene (DNCB) and paranitrosodimethyl aniline (NDMA) in 23 patients with sarcoidosis and 135 control subjects

With PDC, the most potent sensitizer there was no significant difference in the incidence of sensitization in patients with sarcoidosis and in control With DNCB and NDMA, a highly significant decrease in frequency of sensitization was observed in patients with sarcoidosis compared to the controls. Dinitrochlorobenzene was about half as effective sensitizing patients with sarcoidosis as in controls, whereas NDMA the least potent allergen used was about one-fourth as effective.

These findings demonstrate that the lowered incidence of reactivity characteristic of sarcoidosis is not apparent when a strong sensitizer such as PDC is used. It is only with weaker allergens that the difference becomes apparent Actually DNCB and NDMA are considerably more potent than commonly encountered contact allergens, such as formalin, Vioform and heavy metals. Thus a much lower incidence of contact sensitization might be expected in patients with sarcoidosis if these latter compounds were to be tested

Patients with sarcoidosis are capable of reacting to these and other skin test antigens, although the incidence of sensitization is decreased. For this reason the use of batteries of such tests probably has little diagnostic value in sarcoidosis

[This work proves that in sarcoidosis there is diminished capacity to become sensitized or react, not only to tuberculin-type allergens but also to eczematogenic contact allergens.—Eds.]

Experimental Eczema Eczematous Reaction Elicited during Sensitization of Guinea Pig M Golay and R. Brun[9] (Univ of Geneva) administered to the necks of male guinea pigs weighing about 300 Gm. 1 18 daily applications of 1% dinitrochlorobenzene in acetone, and then tested the nipples by application of an 0.1% solution of the same compound at the time of last application to the neck The nipples were excised 24 hours later for histologic study

With the 3d application or 2 days after beginning sensitizing treatment, slight spongiosis was already evident. After 5 days eczematous lesions of the epidermis were observed regularly and were as pronounced as when the tests

(9) Dermatologica 1 ... 408-412, June, 1958

essarily prove stable the test was continued for several weeks, usually 4-6.

Of 88 animals sensitized satisfactorily 25 served as controls and spontaneous variations of threshold were followed in each. Daily subcutaneous injections of 2.5 mg d-amphetamine and 5 mg caffeine were given to 37 animals, and daily injections of 30 mg chloral hydrate to 26 In each group variations in threshold were followed.

Among the controls 13 (52%) of the guinea pigs showed a stable threshold 11 (44%) a slowly rising threshold and 1 (4%) a falling threshold Of the animals treated with caffeine and d amphetamine a stable threshold was observed in 9 (24%) a falling threshold in 26 (71%) and a rising threshold in 2 (5%) Of the animals treated with chloral hydrate a stable threshold was noted in 2 (7%) a rising threshold in 21 (82%) and a falling threshold in 3 (11%) Thus there was heightening of sensitivity by stimulating drugs and lowering of sensitivity by sedatives The drugs used were chosen for their action on the central nervous system particularly at the cortical level and for their lack of peripheral action The effects observed on the threshold of sensitivity could not be attributed to peripheral vascular changes Instead the modification of sensitivity apparently resulted from central nervous system activity effects which could be predicted from *clinical observations and the general laws of cortical function*

These experiments underline the individual character in the development of sensitization its degree and course in the laboratory animal This feature brings the conditions of experiment close to those of contact eczema observed in man The influence of centrally acting drugs on the development of the allergic state shows that the central nervous system modifies the response to the allergen and that it represents an important component of what it is customary to call the soil These conclusions are valid no matter what may be the mechanism determining the eczema and whether or not it is accepted as an antigen antibody reaction

► [With the doses of sedatives or stimulants customarily used in clinical practice in man we *have not* been impressed by any alterations in the severity of allergic contact dermatitis. The doses of drugs given the guinea pigs in these experiments would correspond to the following daily approximate doses in a 150-lb person 375 mg d amphetamine, 0.75 Gm caffeine and 4.5 Gm chloral hydrate!—Eds.]

Induction of Allergic Contact Dermatitis in Patients with Sarcoidosis. William L. Epstein and Robert I. Mayock (Univ of Pennsylvania) determined the incidence of natural

(8) Proc. Soc Exper Biol & Med 94 786-787 December 1957

phene exceeded those to sodium zirconium lactate alone. Acute inflammatory reactions and typical granulomatous lesions also occurred after sub- or intracutaneous injection of sodium stearate. With both sodium zirconium lactate and sodium stearate inflammatory reactions appeared particularly severe around hair follicles. Injection of hexachlorophene alone or a hexachlorophene-diethylene glycol mixture produced moderate inflammatory reactions without necrosis and ulceration.

Percutaneous application of sodium zirconium lactate 9.2% and hexachlorophene, 0.5% in aqueous solution produced acute inflammatory reactions with a tendency to formation of pink papules and nodules. The severity of inflammatory reaction following percutaneous applications was markedly enhanced by defatting the skin, trauma or repeated applications of the test chemicals.

► [These studies fail to answer the important basic question: why do a small percentage of those who use zirconium-containing deodorant sticks develop allergic zirconium granulomas whereas apparently not one person who has used a zirconium-containing cream or lotion for allergic contact dermatitis due to poison ivy has been reported to have developed such granulomas. Is it the different vehicles and other ingredients in these preparations? Preceding trauma by shaving in the axilla? Friction and massaging which are unavoidable in the axilla? Or one of the many other possible differences between deodorant stick and ointment or lotion and between axillae and skin areas usually affected by poison ivy dermatitis? Or perhaps to chemical differences in the sodium zirconium lactate, which is known to possess numerous contaminants in trace amounts. —Eds.]

Induction of Allergic Contact Dermatitis in Patients with Lymphoma Leukemia Complex was attempted experimentally by William L. Epstein[3] (Univ. of Pennsylvania). Two potent sensitizers, 2,4-dinitrochlorobenzene (DNCB) and paranitrosodimethylaniline (NDMA), were applied to the skin of 27 patients with the following diseases: Hodgkin's disease, lymphosarcoma, myelogenous leukemia, lymphocytic leukemia, multiple myeloma and extensive mycosis fungoides. To determine whether sensitization had occurred, the patients were retested 30 days later by a similar application at new sites, with a 1:1000 dilution of each sensitizer in acetone. Because previous studies have indicated that a racial difference exists in the response to contact allergens, the

(3) J. Invest. Dermat. 30:39-40, January, 1958.

were made after additional sensitization applications. No lymphocytic infiltration was found even when the nipple reaction was produced 8-17 days after beginning of sensitization but there was a marked increase of histiocytes. Except in 1 case in which it appeared earlier this histiocytic proliferation did not appear until 5 days after sensitization began.

These experiments show that the "incubation period for an eczema produced at a site of challenge distant from the site of contact sensitization is short, i.e. 2 3 days. Frey and Wenk reported a period of 6-9 days based on macroscopic findings instead of histologic changes.

► [It would be interesting to note whether or not the same very early histologic tissue response would occur at skin sites other than the specialized tissues of the guinea pigs nipples. The absence of mononuclear cells in the cutis and epidermis is noteworthy. Perhaps this is also due to the special site tested. Macroscopically evidence of contact type sensitization usually cannot be demonstrated until after a minimum of 5 days incubation period.—Eds.]

Pathologic Changes Associated with Deodorant Preparations Containing Sodium Zirconium Lactate. Experimental Study is presented by John T. Prior, Herman Rustad and G. A. Cronk[1] (State Univ. of New York, Syracuse). Several zirconium compounds have been used in experimental diagnostic and therapeutic medicine for several years. One of the most important is hydrous zirconium oxide which has been used in large quantities in treating poison ivy dermatitis. To date there has been no evidence of toxicity following use of this preparation. Recently sodium zirconium lactate has been combined with other agents such as sodium stearate, hexachlorophene, alcohol, glycerine, water, perfume and varying amounts of other ingredients and marketed as a deodorant. Reports have appeared of granulomatous inflammatory reactions following use of this type of deodorant for a few days to several months. Sodium zirconium lactate is used in the commercial preparations in 20-25% strength.

The authors found that when injected sub and intracutaneously in rabbits 42% sodium zirconium lactate solution caused marked inflammatory reaction with necrosis of the skin and eschar formation. Reactions following injection of solutions containing 12.6 10.5 8.4 6.3 and 4.2% were similar to those observed with 42% but less severe. Tissue reaction to a mixture of sodium zirconium lactate and hexachloro-

(1) J. Invest. Dermat. 29 449-463 December 195[illegible]

phene exceeded those to sodium zirconium lactate alone. Acute inflammatory reactions and typical granulomatous lesions also occurred after sub- or intracutaneous injection of sodium stearate. With both sodium zirconium lactate and sodium stearate inflammatory reactions appeared particularly severe around hair follicles. Injection of hexachlorophene alone or a hexachlorophene-diethylene glycol mixture produced moderate inflammatory reactions without necrosis and ulceration.

Percutaneous application of sodium zirconium lactate 92% and hexachlorophene 0.5% in aqueous solution produced acute inflammatory reactions with a tendency to formation of pink papules and nodules. The severity of inflammatory reaction following percutaneous applications was markedly enhanced by defatting the skin, trauma or repeated applications of the test chemicals.

[These studies fail to answer the important basic question why do a small percentage of those who use zirconium-containing deodorant sticks develop allergic zirconium granulomas whereas apparently not one person who has used a zirconium-containing cream or lotion for allergic contact dermatitis due to poison ivy has been reported to have developed such a granuloma. Is it the different terrain? The different vehicles and other ingredients in these preparations? Preceding trauma by shaving in the axilla? Friction and massaging which are unavoidable in the axilla? Or one of the many other possible differences between deodorant stick and ointment or lotion and between axillae and skin areas usually affected by poison ivy dermatitis? Or perhaps to chemical differences in the sodium zirconium lactate which is known to possess numerous contaminants in trace amounts. —Eds.]

Induction of Allergic Contact Dermatitis in Patients with Lymphoma-Leukemia Complex was attempted experimentally by William L. Epstein[3] (Univ. of Pennsylvania). Two potent sensitizers, 2,4-dinitrochlorobenzene (DNCB) and paranitrosodimethylaniline (NDMA), were applied to the skin of 27 patients with the following diseases: Hodgkin's disease, lymphosarcoma, myelogenous leukemia, lymphocytic leukemia, multiple myeloma and extensive mycosis fungoides. To determine whether sensitization had occurred the patients were retested 30 days later by a similar application at new sites, with a 1:1000 dilution of each sensitizer in acetone. Because previous studies have indicated that a racial difference exists in the response to contact allergens, the

(3) J. Invest. Dermat. 30:39-40, January, 1958.

Negro (10 patients) and white (17 patients) groups were evaluated separately

Sensitization to both DNCB and NDMA was markedly reduced in patients with the lymphoma leukemia complex. Reactions were observed in 31% of the white patients with DNCB and 6% with NDMA In the white controls 83% reacted to DNCB and 70% to NDMA. In the Negroes with lymphoma leukemia complex, 10% reacted to DNCB and 30% to NDMA Reactions occurred in 61% of Negro controls with DNCB and 45% with NDMA In all only 2 white patients (12%) reacted to both allergens whereas the expected frequency among healthy persons is 64 % for whites and about 35% for Negroes Also the intensity of sensitization as indicated by the degree of inflammation was depressed in patients with lymphoma leukemia complex. Not 1 patient had a patch test reaction greater than 2+ and most showed weak, borderline reactions.

The diminished susceptibility to contact sensitization corresponds with the lowered reactivity shown by these patients to other delayed type antigens. The significance of this diminished capacity for delayed reactivity is not understood The most popular explanation is that the cells responsible for producing delayed antibodies" are crowded out by neoplastic nonantibody forming reticulum cells However this concept must remain a speculation as long as the site of synthesis of delayed antibodies is unknown

Effect of Feeding Simple Chemical Allergens to Pregnant Guinea Pigs on Sensitizability of Their Offspring was studied by Rudolf L. Baer Stanley N Rosenthal and Blanka Hagel[3] (New York Univ Post Grad Med School and Skin and Cancer Unit) Groups of pregnant albino guinea pigs were force fed olive oil solutions of picryl chloride (PC) or dinitrochlorobenzene (DNCB) Pregnant control animals were fed olive oil alone Several weeks after birth the offspring were sensitized to the allergen fed the mother After a 4-week incubation period all guinea pigs were simultaneously tested with dilutions of the allergen to which they were sensitized Offspring born to animals fed solutions of PC or DNCB during gestation had a slightly though consistently lower capacity to become sensitized to the homologous allergen than did the offspring of mothers not fed the

(3) J Immunol. 80 429-434, June 1958.

allergen. In 17 of 18 test ites with different dilutions, the averages of the reactions of the offspring of allergen-fed mothers were weaker than those of the control animals off spring

The authors inf r that the feedings of the allergen to the pregnant guinea pigs may ha e had a slight effect on the sensitizability of the offspring Th s i supported by results of deliberate sensitizations to citraconic anhydride, a chem ically unrelated substance, n the same animals. With this compound there was no uniform trend toward lesser sensi tizability n either the test animals born of mothers exposed to one of the two oth r allergens or the control animals Fur ther the differences between test and control animals in the averages of the reactions to citraconic anhydride were less tha those noted between the test and control animals sensitized to PC and DNCB This also suggests that the dif ferences observed in the sensitizability of animals born to allergen-fed mothers and control animal are based on a pe cific effect rather than on chance. The result of these exper iments are not conclu ive but they are sufficiently suggestive f some pecific lessening of sensitizability to encourage further stud es in thi mportant field of in estigation

[These results are suggestive of slight inhibition of sensitizability and are not conclusive evidence that specific acquired tolerance was produced. However recently it has been found also that guinea pig fetuses injected with tuberculin have diminished susceptibility to become sensitized to tuberculin in adult life as compared with control animals

The findings of the authors ith simple chemical contact allergens and of Weiss (J Exper Med 10 83 1958) with tuberculin lend further evidence to the "marker" theory of Burnet H attempted to explain why animals do not form antibodies against their ow antigenic tissues, even though they do so against the tissues of other animals According to this theory animals in fetal life learn to recognize and "mark" their body-own mate rials as peculiarly their ow and therefore they fail to form antibodies against them in postfetal life He theorized that this mechanism might apply even to entirely foreign materials as long as exposure to them took place accidentally or deliberately during fetal lif —Eds]

Experimental Toxic and Allergic Contact Dermatitis.— *Chemical study of histamine co t at*—Using an adaptation f the microchemical m thod of Lowry nd co-workers J Procha ka F ber a d R bert A Cooke (Roosevelt Hosp., New York) with the technical assistance of Sonya Str sman and Gloria Gordon found the histamine content of normal guinea pig sk t be 2-6 µg (verage 4.3 µg) At the tes f allergic dermatiti n sensiti ed guinea pigs

(17) J Allergy 29 394-416, September 958

after epicutaneous application of 0.1% dinitrochlorobenzene (DNCB) a steady rise in histamine was observed beginning after the challenge and reaching a maximum at 48 hours. At this time the histamine content averaged over 400% above normal. Insignificant changes were observed in the histamine content of lesions of toxic dermatitis induced in normal guinea pigs by application of 2% DNCB but in those induced by 5% DNCB the histamine content increased to a maximum about 80% above normal 48-72 hours after application. Thus the increase in histamine content was much less than that observed in allergic dermatitis.

The infiltrating cells observed in guinea pigs with experimental allergic dermatitis were mononuclear cells whereas in toxic dermatitis they were both polymorphonuclear and mononuclear cells in about the same proportion as found in blood. There was no significant difference in the number of cells found at the sites of allergic dermatitis due to 0.1% DNCB and toxic dermatitis due to 5% DNCB. Leukocytes in normal and sensitized animals contained the same amount of pre-formed histamine and no significant changes in the histamine content of whole blood were observed during or after an allergic reaction. The qualitative cellular difference in the infiltrate at the sites of toxic versus allergic dermatitis seems too small to explain the marked difference in histamine levels in the two different inflammatory reactions. Thus it may be assumed that the infiltrating mononuclear cells of sensitized animals have the capacity on minute specific stimulation with an antigen to activate histamine metabolism at the site of an allergic inflammation by promoting histamine synthesis, inhibiting histamine breakdown, or both.

Much less histamine was found in allergic lesions of guinea pigs given injections of germanin. Apparently germanin, an inhibitor of histamine formation from l-histidine, interferes with decarboxylation at the site of allergic dermatitis. This supports the assumption that the histamine accumulation in allergic dermatitis is induced by activation of histamine metabolism. Allergic lesions in guinea pigs given injections of germanin lasted much longer than allergic lesions in animals not given this drug. This suggests that histamine is an accelerator in the repair process rather than a causal factor in these allergic reactions.

II Histopathologic study.—Fisher and Cooke,[3] with the technical assistance of Stroyman and Gordon, induced toxic dermatitis in normal guinea pigs by application of 5% DNCB. Allergic dermatitis resulted from application of 0.01 or 0.1% DNCB to the skin of guinea pigs sensitized to this chemical. The 3-12 hour lesions of toxic dermatitis showed epidermal injury always accompanied by scant extravasation of polymorphonuclear and mononuclear cells. The 3-12 hour lesions of allergic dermatitis showed massive extravasation of mononuclear cells migrating in trails directly into the epidermis. Thus, the concentrated chemical caused relatively sparse infiltration in the toxic reaction whereas dilute DNCB induced massive infiltration with direct ascent of the mononuclear cells toward the challenged skin surface. The most plausible explanation for the behavior of the mononuclear cells seems to be that the sensitization induced in them a capacity for positive chemotaxis, i.e. a faculty for detection of a chemical (or its protein derivative) in minute concentrations and for migration straight into the area of highest concentration.

Most toxic lesions at 24-48 hours showed an increase of polymorphonuclear and mononuclear cells in the dermis after the earlier death of epidermal cells. Allergic lesions at 24-48 hours showed massive invasion of the epidermis by mononuclear cells and formation of vacuoles. In some lesions microvesicles formed, presumably at points of fusion of vacuoles. Vacuolation and vesiculation cause disruption of the epidermis apparently leading to its death and exfoliation. Mononuclear cell invasion, vacuolation, vesicle formation and exfoliation of the epidermis are steps in a process characteristic of the allergic response not seen in toxic lesions. Histamine accumulation and increased phosphatase activity also occur in allergic but not in toxic lesions. Thus allergic reaction shows not only a specific cellular response but also a characteristic intensity in local metabolic activity, enzymatic in character.

The results suggest that the allergic reaction depends on mononuclear leukocytes which acquire specific capacities through sensitization. However histologic findings at sites of allergic dermatitis in guinea pigs given injections of germanin indicate sensitization also of epidermal cells. In all

[3] J Allergy 29 September 1 38

animals treated with germanin the 48-hour allergic lesions revealed considerable dermal infiltration by mononuclear cells. However the epidermis was extremely thickened and *not invaded by these cells It seems that germanin prevents* ascent of the mononuclear cells in the epidermi The extreme epidermal thickening might be regarded as the allergic response of epidermal cells after participation of the mononuclear cells has been forestalled

► [These findings confirm the observations in guinea pigs of our group (J Invest. Dermat. 27 249 1956, and A.M.A. Arch. Dermat. 76 549 1957) Jadassohn s group (Acta dermat. venereol 36 360, 1956, and Dermatologica 114 91 1957) and Nilzen s group (Acta dermat. venereol. 35 292, 1955)

The new finding is the striking increase in histamine content of allergically reacting skin and much less striking increase in skin reacting on a primary irritant basis The explanation that the monocytes of sensitized animals have the capacity to activate histamine metabolism at the site of an allergic inflammation is not likely to be correct as our own studies have shown that the type of damage occurring in primary irritant reactions is in principle different from that seen in the allergic response. One is a primarily *parenchymatous reaction* and the other *is* one of *intercellular edema* Since the intercellular edema appears even before masses of mononuclear cells have arrived in the intercellular spaces in the epidermis, the mononuclear migration probably is a consequence rather than a cause of the changes. This makes it unlikely that the mononuclear cells are the immediate cause of the increase in histamine content.

The very significant effect of germanin on the allergic response to DNCB also is a new finding. The mechanism which produced the acanthosis in the animals given injections of germanin at the DNCB sites needs further elucidation, before one can accept the interpretation that the acanthosis is an altered form of allergic epidermal response —Ed]

Influence of Selenium Disulfide on Sebaceous Gland Volume in Guinea Pigs *was investigated by Erik Skog*[6] (Univ of Cincinnati) Guinea pig skin was exposed to selenium disulfide shampoo (Selsun®) and to the shampoo vehicle only Shampoo treatment was repeated 10 times at intervals of 2 3 days Biopsy specimens were excised before and after the course of treatment and the volume of the sebaceous glands was determined as described by Rothman and associates

Selenium disulfide shampoo and the shampoo vehicle alone caused considerable increase in the volume of sebaceous glands, but the effect of the selenium shampoo was more pronounced Treated epidermis was thicker than untreated epidermis. The latter had 3 or 4 cell layers whereas treated epidermis had 5-9 layers Most of the cell proliferation was confined to the prickle cell layer Such acanthogenic action is also exerted by various kinds of detergents The shampo

(6) Acta dermat. venereol 38 15 19 1958

contains a high percentage of Nacconol* an alkyl benzene sulfonate detergent having marked acanthogen c activity. The effect was not confined solely to the superficial layers of the epidermis but occurred also in the follicles which became much wider than normal. Synthetic detergents may exert th same hyperplastic action on the sebaceous glands as they do on the epidermis. The results of the investigation suggest that the effect is potentiated by selenium disulfide.

► [This investigation provides possible explanation for the excessive oiliness of the scalp and scalp hair which occurs in about 30% of persons who shampoo ith Selsun Suspension Recently Sulzberger called attention to the apparent increase in the incidence of somewhat patterned diffuse alopecia of the scalp in young and middle-aged women. During recent years this type of hair loss has been noted with increasing frequency by many dermatologists in the United States and Europe. Of course, many possible etiologic factors hav been considered, g the prolonged and repeated exposure to the acanthogenic action of certain detergents in Sel sun and many other shampoos which ha been sold during the past 10 years or so But neither thi nor the nylon brushes reported on by Sa ill (see p 267) are likely to be the causative agents of this particular type of thinning of the scalp hair —Eds]

Effect of Temperature on Production of Herpes Simplex Virus in Tissue Culture was in estigated by Clayton E. Wheeler[7] (Uni of Virginia) Cultures of HeLa and AU cells infected with 3 strains of herpes simplex virus and in cubated at 4 different temperatures for 3 days were observed for cytopathogenic effects a d t trated fo irus content. Littl no rus production was found in cultures incu bated t room temperature (20 5-27 7 C) Greater amounts of viru were produced at 30 and 40 C and the greatest amount wa produ ed at 35 C Cultures of H La cells which were in cubated at room temperatu e and howed little or no evi dence of irus prod ction (few o no herpes plaques and little or no t tratable v rus) promptly produced ncreased amount of irus when the incubation temperature was raised to 35 C I ubation of herpes ru m blanks (culture t bes contai ng med um but no ll) at 40 C resulted in complete los f ru Small amount of virus survived in cubation t 35 C more surv ed t 30 C and the greatest amount rv ed at room temperat e

Present data show that ncubation temperature has a profound ffect on the amount of herpes irus present in pooled cell and medium at the end of 3 day ncubation Stud es of rus-host y tem ther than those in olving herpes im

7) J Immunol 81 98 105, July 958

plex indicate that temperature has an important effect on the amount of virus produced. In a number of animal virus host systems the optimum temperature range is 35-37 C. (influenza yellow fever vesicular stomatitis myxoma, vaccinia, variola and ectromelia) and higher incubation temperatures result in less virus production or its cessation It is not clear in most instances whether the lower yield of virus at higher temperatures is due to greater virus inactivation or to less virus production or a combination of both All animal virus host systems do not respond identically to variations of temperature and plant virus host systems show considerable variation in optimum temperature of incubation.

Results of the present study might apply to the problem of recurrent herpes simplex infections in man following elevation of body temperature. Elevation of body temperature increases the temperature of skin cells If a few of these skin cells contain herpes simplex virus in some form (*latent or inapparent infections*) a temperature rise might result in temporary increased production of herpes virus which becomes manifest as the clinical disease The mechanism of recurrent herpes simplex infections probably is not this simple but the possibility provides an entering wedge for *further study*

► [The great variety of factors known to precipitate recurrences of herpes simplex lesions makes it likely that several mechanisms produce these recurrences. Wheeler's work suggests at least one possible mechanism, since the local increases in temperature resulting from trauma, sun exposure, inflammatory processes, allergic reactions, etc., may be one of these trigger factors for recurrent herpes simplex.—Eds]

Long term Tissue Culture of Epithelial Like Cells from Human Skin. Clayton E Wheeler Charles M Canby and Edward P Cawley (Univ of Virginia) after incubation of trypsinized material from human skin for 31 days found a small colony of epithelial like cells in one of the tubes The cells continued to multiply A few were removed 45 days after planting and transferred to other tubes where they continued to multiply *rapidly and maintain an epithelial like* appearance. The cells have been grown continuously for 9 months and 30 subcultures have been made An enormous number of cells has been grown from the original colony The medium used for growth was 40% pooled human serum 5% chick embryo extract and 55% balanced salt solution con

(8) J Invest. Dermat. 29 383 392, *November* 1957

taining 100 units of penicillin and 100 µg streptomycin/cc.

The line of cells (referred to as AU cells) when grown on cover slips and stained with hematoxylin and eosin, resembled so closely those of epidermoid carcinomas of anaplastic type as to be indistinguishable. The AU cells showed variations in size, shape and staining qualities. Mitotic figures and abnormal mitoses were frequent.

The AU cells resemble HeLa cells in their rapid growth and ease with which they can be transplanted. Microscopically most AU cell cultures are indistinguishable from those of H La cell m the unsta ned and stained states. The AU cells, however are not quite as stable or fast growing as HeLa cells

The ew AU cell line supports the growth and multiplication of three strains of herpes simplex virus Vaccinia virus has also been shown to proliferate in AU cells but the authors have been unable to demonstrate cytopathogenic change in AU cells after addition of the virus of ecthyma contagiosum or of tissu from a milkers nodule.

The isolation of cells having the morphologic characteristic f malignant cells in tissue culture from normal human tis ue has been reported by a number of authors. Cells with growth and morphologic haracteristics similar to those of AU cells have been isolated from normal skin conjunctiva, foreskin, appendix, intestines kidney liver bone marrow and nasal mucosa. Although the cells of these lines grow rapidly how increased capacity for anaerob c glycolysis and ha morphologic characteristics of malignant cells, they ha e not been proved to be actually mal gnant.

The exact sit or cell of origin of the various cell lines s unknown. Their morphology suggests an epithelial origin, but thei tissue sources do not xclude origin from connec tiv tis u blood essels rve sheaths o other structures. Whether these ell represent m tations from normal cells, whether something n the growth medium exerts a carcinogenic ffect o whether ther re inhibitor substances in the intact an mal not p esent in tro that prevent malig nant hanges are unexplored pos bil ties.

► [The results observed by Wheeler Canby and Cawley pose many questions Of course, there is big difference between tissue culture skin cells and cells in the living human skin Nevertheless, one must suspect that perhaps epidermal cells ar more pluripotential than orthodox teaching would permit one to believe and that possibly some or many or all cells

of the skin (and other organs?) have the potential for malignant changes and that it is certain growth-controlling (inhibitory) factors present in living skin which prevent malignant changes from supervening. The latter possibility no longer seems so farfetched in view of the finding of the Sloan Kettering Institute group that patients with malignant tumors have a distinctly decreased resistance to growth and invasion by cultured malignant cells as compared with subjects without malignant tumors.—Ed.]

Evidence for Humoral Mechanism Which Prevents Growth of Dermatophytes in living tissues below the water electrolyte barrier of the skin is presented by Allan L. Lorincz, Joseph O. Priestley (Univ. of Chicago) and Paul H. Jacobs* (Walter Reed Army Hosp.). Small inocula of *Trichophyton mentagrophytes* were placed inside sterilized dialysis bags which were then implanted intraperitoneally into 10 mice. At intervals of 1, 2, 3, 4, 5 and 12 weeks, respectively 1, 1, 3, 1, 2 and 2 of the bags were removed and examined. There was no evidence of severe tissue reaction around any of the bags, and in none was there any evidence of growth of the fungous inocula. Similar control dialysis bags prepared at the start of the experiment and placed in Sabouraud's medium or normal human serum all showed vigorous fungous growth in less than 2 weeks. Even after 12 weeks in the peritoneal cavities of mice, when the original inocula were removed from the dialysis bags and planted on Sabouraud's medium, vigorous growth of the fungus occurred. Apparently, a humoral factor is involved in the suppression of dermatophytic growth in the living tissues of the mouse which is dialyzable and hence not ordinary protein antibody, either natural or acquired.

Dialysis bags containing suspension of *T. mentagrophytes* were placed in 10 small sterile test tubes and 1 cc. sterile serum from a healthy donor was added to each tube. In 5 tubes the serum was removed daily and replaced with fresh serum from the same donor. All tubes were placed on a shaker to keep their contents in circulation. After 3 or 4 days, fungous growth appeared in all 5 tubes in which the serum was not changed. Of the 5 tubes in which the serum was changed daily, growth failed to occur in 3, even after 3 weeks, whereas in 2 it appeared on the 5th day and was slow and inhibited for another 3 days. When the experiment was repeated using serum which had been frozen, there was no inhibition of fungous growth even in tubes in which the serum was changed twice daily.

(9) J. Invest. Dermat. 31:15-17, July, 1958.

On the basis of these in vitro experiments, the demonstration of an antidermatophytic, dialyzable substance in human serum is still slightly equivocal and further studies are needed. Nevertheless, it is felt that there is highly sugges ti e evidence f r the existence of some dialyzable water sol ble unstabl substance in serum and tissue flu ds which suppresses the growth of d rmatophytes and permits them t thrive only n those areas of the host not reached by uch flu ds

► [Interesting findings which help explain why superficial fungi remain superficial. Studies such as these should be extended as they could add considerably to our knowledge concerning human susceptibility and defense to disease —Eds]

Esterases in Cutaneous Granulomas. G C Wells (Univ f London) xamined histochemically specimen of normal and path logic skin in many dermatoses, ncluding chronic granulomas. Strong alkaline phosphatase activity was noted in the l ngs of kin capillaries, n the troma of papillae of growing ha rs and in fibrocytes and young connective tis ue fiber f sca tissue Acid phosphatase was con istently present in all epithelial structures of th kin with some intensi fication of concentration at the keratogenou zones. In tu berculoid infiltrates acid phosphatase was diffusely present with somewhat greater concentration in giant cell and epi theliod cell masses, but was also p esent in lymphocytic masses and various infiltrates unrelated to infection

With th methods of Holt there appeared to be no simple esterase acti ty n normal epidermis and its keratin layer except at the mouths of some pilosebaceous follicles and in the intraepidermal portio s of some weat ducts. Some aci na cell f weat glands howed strong esterase activity in ontra t to adjacent acina cells or other sweat glands, which might how none Sweat ducts contained a variabl amount of impl esterase n thei lumens The hea iest concentra tion of th non pecifi esterase n norm l skin wa in the pilosebaceou f llicles at the point at wh h the sebum entered the ha haft canal The sebaceou glands themsel es appeared to be esterase negati e.

The most con tently esterase-posit e elements of the skin wer the scattered dendrit ll of the derm These histiocytes become more prom nent through increase n their esterase content in many hron c nflammatory cond tions,

[1] Brit J Dermat. 69 437 December 1957

of the skin (and other organs?) have the potential for malignant changes and that it is certain growth-controlling (inhibitory) factors present in living skin which prevent malignant changes from supervening. The latter possibility no longer seems so farfetched in view of the finding of the Sloan-Kettering Institute group that patients with malignant tumors have a distinctly decreased resistance to growth and invasion by cultured malignant cells as compared with subjects without malignant tumors.—Eds.]

Evidence for Humoral Mechanism Which Prevents Growth of Dermatophytes *in living tissues below the water* electrolyte barrier of the skin is presented by Allan L. Lorincz, Joseph O. Priestley (Univ. of Chicago) and Paul H. Jacobs[9] (Walter Reed Army Hosp.). Small inocula of Trichophyton mentagrophytes were placed inside sterilized dialysis bags which were then implanted intraperitoneally into 10 mice. At intervals of 1, 2, 3, 4, 5 and 12 weeks respectively 1, 1, 3, 1, 2 and 2 of the bags were removed and examined. There was no evidence of severe tissue reaction around any of the bags and in none was there any evidence of growth of the fungous inocula. Similar control dialysis bags prepared at the start of the experiment and placed in Sabouraud's medium or normal human serum all showed vigorous fungous growth in less than 2 weeks. Even after 12 weeks in the peritoneal cavities of mice, when the original inocula were removed from the dialysis bags and planted on Sabouraud's medium, vigorous growth of the fungus occurred. Apparently, a humoral factor is involved in the suppression of dermatophytic growth in the living tissues of the mouse which is dialyzable and hence not ordinary protein antibody, either natural or acquired.

Dialysis bags containing suspensions of T. mentagrophytes were placed in 10 small sterile test tubes and 1.5 cc. sterile serum from a healthy donor was added to each tube. In 5 tubes the serum was removed daily and replaced with fresh serum from the same donor. All tubes were placed on a shaker to keep their contents in circulation. After 3 or 4 days, fungous growth appeared in all 5 tubes in which the serum was not changed. Of the 5 tubes in which the serum was changed daily, growth failed to occur in 3 even after 3 weeks, whereas in 2 it appeared on the 5th day and was slow and inhibited for another 3 days. When the experiment was repeated using serum which had been frozen, there was no inhibition of fungous growth, even in tubes in which the serum was changed twice daily.

(9) J. Invest. Dermat. 31:15-17, July, 1958.

Histologically the true keloid is believed to be a benign connecti e tissue tumor Though it feels hard, it is often edematous and contains thin connective tissue fibers and young fibrocytes.

Investigations into Cantharidin Blisters Raised on Apparently Normal Skin in Normal and Abnormal Subjects. J H. Allison and F Ray Bettley[3] (Middlesex Hosp London) found that patients with atopic eczema had larger blisters containing more protein both absolutely and relative to their own plasma than did normal subjects or patients with other types of eczema of comparable severity Patients with seborrheic hypostatic and nummular eczema had blisters of normal size containing more protein relative to their plasma than did normal subjects. Patients with urticaria had blisters of normal size, absolute protein content and protein content relative to their own plasma.

Blister lids removed from patients with atopic eczema 20 hours after pplication of 0.2% cantharidin showed many acantholytic cells of a type rarely seen in blister lids from noneczematous subjects. The blood leukocyte count was higher than normal n patients with widespread atopic ecze ma. Bli ter fluid white cell counts were below normal in patients with less than 15% of the skin affected by atopic eczema, possibly due to e cessi volume of blister fluid for mation.

Blister fluid n cantharidin blisters may originate from the capillaries or from damaged epidermis. If blister protein comes mainly from the cap llaries, cantharidin must produce greater vascular permeabil ty in atopic and eczematous pa tients tha n no rmal The fact that patients with urticaria howed blister w th normal protein content, although vas cular permeability is likely to be more easily produced in thi group suggest that the increased permeab l ty in ecze ma and topy i due to the action of cantharidin on the essel being m d fied by an altered epidermis. H stologic t dies f blister l ds indicat some d fference in the degree of acanthol y in the eczema and atopic groups as compared to the control group For these easons, the authors con lude that n th t pic and eczema groups the epidermis of apparentl normal kin i mor read ly damaged by can tharid tha t the skin f a normal person The fragil ty is

3) Brit J Dermat 70 331 339 October 958.

such as lichenification warts hyperplasia and acne *keloid* In chronic cutaneous granulomas, macrophages and giant cells were found *to be rich in simple esterase whereas epi*thelioid cells plasma cells and lymphocytes had more Lepra cells were strongly esterase positive.

This survey of hydrolyzing enzymes in cutaneous lesions diverts *attention* from the relation between these enzymes and infecting organisms (except insofar as the lepra cells are *rich in nonspecific esterase*) Instead attention is focused on the histiocytes or macrophages which are seen to be heavily loaded with simple esterases in various chronic infections and noninfectious granulomas. These cells are di*stinct from epithelioid and other cells of chronic inflammatory* infiltrates and when histochemical methods for estera es have been used their morphology is clear It is not known what chemical part these histiocytes play in the metaboli m of foreign material or of damaged tissue.

Studies on Keloid Tissues were conducted by F r Woringer and J Zimmer[2] (Univ of Strasbourg) The keloid is not a uniform fibrous tissue Various morphologic characteri tics indicate a young connective tissue with active fibrocytes which develop well in edematous surrounding The keloid *appears to be rich in water which is bound to the ground* substance the latter i different from that of the normal cutis Using the McManus stain the keloid shows heavier stain ing in the areas of edematous connective tissue than the adjacent normal cutis Electron microscopic studies of keloid tissues also revealed an increa e of ground ub tance over that of the cuti

The authors *did paper chromatographic tudie on kel id* and normal kin tissues in an effort to c mpare in both the amount of alcohol soluble and ether insoluble amin acid containing substances (amino acid and peptide) Nonhydrolyzed alcohol extract were u ed whi h fixe l all cell and fibers.

Certain cysteine acid compound (c steine r homocysteine) are present in unbound *form in the uti and in bound* form in keloid tissue also the cuti ontain m re peptides and fewer amino acids than the keloid ti sue The peptide of the two *tissues* seem to be different in quality Moreover keloid tissue is able to retain more fluid than the cuti

(2) Hautarzt 9 341 344, August, 1958.

minum salts which are used as deodorants were studied 100-500 µg was required to inhibit growth of the micro-organisms commonly found in the axillae.

► [Based on the premise that bacteria act on axillary secretions to produce body odor this study demonstrates the effectiveness of hexachlorophene as deodorant. Of the various substances tested, hexachlorophene was particularly effective in inhibiting the growth of bacteria even when used in the most minute concentrations —Eds]

Effect of Water-Soluble Constituents of Horny Layer of Skin on Bacteria First Report. H Rockl H W Spier and G Pascher[3] (Univ of Munich) investigated the mechanism of bacterial resistance (auto-disinfection) of the skin surface First, the water-soluble constituents of the superficial horny layer were studied using as culture mediums (1) the watery eluate of the scrapings of the superficial horny layers of healthy persons, which was used in unheated and heated (inactivated) form and (2) artificial culture mediums which contained in various combination the chemical components such as the anions cations, urea and amino acids found in the watery eluate of the horny layer

The natural eluate was studied at the usual pH of the normal skin surface pH 5 whereas the artificial mediums were kept at pH 5 7 and 8. The following bacteria were tested on the mediums described Staphylococcus aureus (coagulase-positive) Staph. albus enterococcus, Escherichia coli and Pseudomonas pyocyanea The natural eluate proved bactericidal for all bacteria. This was probably due to a so-called high concentration effect and not to the presence of certain antibiotic substances.

Of the artificial mediums the addition of a pyrrolidone carbonic acid to the mixture of anions cations, NH and urea proved relatively strongly bactericidal for the three types of [illegible] The mixture of amino acid only proved relatively bactericidal for the two types of staphylococci and for E coli The artificial medium showed less bactericidal effect than the natural eluate This may be due either to the possibility that the natural eluate contains substances not [illegible] defined chemically or to the method of preparing the artificial medium [illegible] the heated natural eluate showed some similarities in its bactericidal effect to the basically heat resistant artificial mediums.

[3] Arch. klin. u. exper. Dermat. 205:420-34, 1957

much greater in patients with atopic eczema than in those with seborrheic nummular or hypostatic eczema.

► [The question is whether the normal-appearing skin of patients with atopic dermatitis is really "normal. Our clinical experience leads us to doubt this, except perhaps in the very mildest cases. Is vascular permeability really more likely to be produced in patients with urticaria than in patients with other dermatoses?—Eds.]

Water Content of Stratum Corneum IV Importance of Water in Promoting Bacterial Multiplication of Cornified Epithelium *Irvin H Blank and Ruth K Dawes*[4] (Harvard Med School) describe a method which permits determination of the moisture content threshold below which a sheet of cornified epithelium will not support growth and multiplication of micro-organisms Four representative organisms were studied Micrococcus pyogenes var aureus a nonpigmented micrococcus of the type often found on the cutaneous surface a coliform bacillus and a diphtheroid The moisture requirement for the two micrococci was the same a moisture content of 23 mg /100 mg prevented growth whereas 29 mg /100 mg allowed growth. Growth of the coliform bacillus was prevented when the cornified epithelium (callus) contained only 36 mg /100 mg but was permitted by a moisture content of 50 mg /100 mg Diphtheroids failed to grow when the moisture content was 50 mg / 100 mg but grew readily when the content was 70 mg /100 mg These *findings indicate that dehydration of the skin* resulting from lower relative humidity of the environment might be expected to cause earlier disappearance from the skin surface of diphtheroids and coliform bacilli than of cocci Apparently the range of optimal moisture content of the cornified epithelium is narrow If there is too much moisture the bacterial population increases if too little the skin feel dry

Using hydrated callus as a culture medium the authors determined the amount per unit area of various topical antiseptics required to inhibit growth of M pyogenes var aureus Less than 0.1 µg neomycin sulfate/sq cm callus prevented growth of this organism but more than 5 µg bacitracin was required. Growth of the micrococcus on hydrated callus was inhibited by 1 µg hexachlorophene or 100 µg benzalkonium chloride. No inhibition of growth was observed from 10 µg boric acid but 100 µg caused some inhibition Various alu

(4) J Invest. Dermat. 21 141 145 September 1

bases indicating that the anesthetic penetrates via the follicle. The author believes that the drug passes laterally through the follicular wall at a level near or just below the lower level of the external barrier and goes through the stratum mucosum to reach the papillary portion of the dermis Edema at this point would account for the perifollicular whealing

► [It could be of both theoretical and practical importance to know more about the depth and degree of anesthesia resulting from these topical applications Is anesthesia to needle pricks sufficient to allow for scalpel or punch biopsy of an area or for electrodesiccation and curettage of localized lesion? If so this method of anesthesia might be ideal for the management of selected lesions in children and perhaps even in some adults On the other hand, it would be interesting to know if such external exposure to the local anesthetics tends to result in higher incidence of allergic sensitization than intracutaneous injection —Eds]

Location of Superficial Epithelial Barrier to Skin Penetration. Samuel Monash (Univ of Miami) compared the percutaneous penetration of topical anesthetics antihistamines and histamine in intact skin and skin in which selected levels of epithelium were exposed by stripping off cells of the stratum corneum with cellophane adhesive tape Biopsies of the exact sites stripped and tested physiologically were performed to determine the amount of stratum corneum that had been removed

A comparison of the time required to produce anesthesia in normal skin and on skin stripped 15 times (thus removing about half to two thirds of the stratum corneum) showed a diminution with 2% Dorsacaine 2% Xylocaine and 2% Pontocaine base solutions of 70 55 and 45 minutes, respectively With 5 more strippings, the further diminution in time was negligible. The outer 15 strippings, therefore, form the principal barrier to penetration of the 2% base solutions Similarly with the hydrochlorid solutions of these anesthetic drugs stripping the skin 15 times resulted in removal of the main barrier to penetration. The rest of the stratum corneum offered little resistance to passage of the solutions

Histamine phosphate concentrations equivalent to 1:5000 of the base when applied to intact skin failed to produce a detectable effect On the forearm 10 strippings failed to remove the barrier but after 15 strippings histamine produced recognizable changes

The author concludes that the superficial barrier to per

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Topical Anesthesia of Unbroken Skin was produced by Samuel Monash[6] (Univ of Miami) in 45 minutes to 1 hour by application of 2% anesthetic base solutions in an alcoholic solvent under an occlusive dressing Drugs used were lidocaine (Xylocaine®) tetracaine (Pontocaine®) phenacaine (Holocaine) procaine, benoxinate (Dorsacaine®) and tripelennamine (Pyribenzamine®) The solvent contained 45% isopropyl alcohol 10% glycerin and 45% water Procaine base required a much longer time to produce anesthesia. Similar anesthesia was produced in 1½ hours with 5% anesthetic bases in hydrophilic ointment or petrolatum Both alcoholic solution and ointments produced anesthesia lasting an average of 2-4 hours.

Partial anesthesia after 4 hours was produced with 5% anesthetic salts (lidocaine phenacaine and tripelennamine hydrochlorides) respectively in hydrophilic ointment or petrolatum No anesthesia was obtained after 5 hours with procaine hydrochloride. With 2% anesthetic salts in aqueous solution anesthesia was produced by the well method (wall of petrolatum surrounding a pool of anesthetic solution) of continuous contact in 2 2¼ hours Anesthesia of the palmar surface was produced with 25% benoxinate base in an alcoholic solvent after a 4-hour application

Pretreatment with ethyl chloride spray for 15 seconds followed by an occlusive dressing of 2% lidocaine base in alcoholic solvent produced anesthesia in 30 minutes on the forearm compared with the usual 45-60 minutes required without such preliminary treatment. The addition of 1% sodium hydroxide *to 2% benoxinate base in alcoholic solvent* resulted in anesthesia in 20 minutes The application was removed after 10 minutes to prevent injury to the skin by the sodium hydroxide

A certain concentration of anesthetic substance in the skin is required to produce anesthesia A concentration sufficient to induce anesthesia would seem to be better obtained with anesthetic bases than with solutions of salts because of the greater rapidity with which the more soluble salts are removed by the circulation It has been shown that free bases are lipid soluble, penetrating the skin at a greater speed than salts

Perifollicular whealing is observed with some anesthetic

(6) A.M.A. Arch. Dermat 76:752-756, December 1957

Studies of embryonal hemopoietic function in subcutaneous fatty tissue has not definitely confirmed Chevremont's conclusions that the fatty tissue represents a latent stage of hemopoietic tissue. Blastic nuclei were found in the hypodermis of embryos. These coexisted with hemopoietic foci in the dermis; structure of fatty tissue was completely preserved, and the hypodermic hemopoietic foci were usually pericapillary and probably related to the polyblasts of the capillary perithelium.

Existence of hemopoiesis in the dermis mesenchyma, observed in all areas examined, justifies the conclusion that in other organs besides the skin the mesenchyma possesses the capacity of creating blood differentiations during certain stages of embryonal development, and the possibility that this capacity may be revived in pathologic conditions later in life. Other investigators have already shown hemopoietic function in pulmonary tissue of the human embryo. Pathogenic mechanisms and etiologic factors which may determine pathologic revival of latent dermal hemopoietic function raise clinical and physiopathologic problems of great importance.

► [If there is latent hemopoietic dermal function which could be revived under certain conditions this would indeed be of the greatest clinical and physiopathologic importance. Apparently 1 of every 200 cells in the epidermis is a small round cell (Andreassen, E.: Acta dermat.-venereol. (supp. 29) 32: 17, 1952). The assumption has been that these small round cells are lymphocytes derived from the blood stream. Although this is supported by the beautiful studies of Hagerman (Acta dermat.-venereol. 34: 51, 1954) there is no proof that all or even most lymphocytes seen in the skin actually are derived from the circulating blood. The eosinophil is another cell which perhaps can be formed locally in the skin.—Eds.]

Experimental Studies on Behavior of Hyperplastic Rat Epidermis were conducted by Gerd Klaus Steigleder and Waldemar Buchwald[3] (Univ. of Frankfort). The way hyperplasia of the rat epidermis develops depends on whether ointment has been applied once or several times. The reaction of the epidermis to white petrolatum is not specific, but also applies to other ointment bases and probably to rubbing alone. There are only quantitative differences in epidermal response. Epidermal hyperplasia could be prevented by chloroquine.

The authors investigated the effect of white petrolatum on the rat epidermis, which had been made hyperplastic by tea-

(3) Hautarzt 8 515 523 November 1957

embryos and fetuses from 2 months after conception to term *showing participation of the skin in hemopoietic function* during successive stages of development of the hemopoietic *system* *All* regions of the skin were investigated

Dermal hemopoiesis is *observed in all cutaneous zones, without* exception Embryonal dermis consists of completely undifferentiated mesenchyma until the 2d month of intrauterine life *differentiation appears in embryos 8 cm long* and continues as they grow The first hemopoietic foci are represented almost exclusively by erythroblasts. Initial meg*aloblastic and megalocytic forms are very* definite These are replaced rapidly by typical proerythroblasts and erythroblasts Other differentiations of blood appear later beginning at the 5th *month of pregnancy and are manifested by mixed* hemopoietic sites composed of differentiated blastic cells and mature blood cells Blastic cells *of the red series and erythrocytes* disappear from the skin *in embryos* 44-50 cm long i e during the last 2 months of intrauterine life This is probably due to phagocytosis of these elements by *cells of the white series which appear and develop during* these last 2 months

Transformation of mesenchymatous cells in hemopoietic *nuclei is manifested clearly in all sections except* those taken from fetuses during the last 2 months of gestation This transformation is evident in the form of isolated cells and tho e not yet differentiated *which change into* hemocytoblastic elements At this stage it is difficult especially during the last 2 months of the intrauterine period to follow the ori*gin of blood cells* since the general *hemopoietic system* is already advanced at this stage Perivascular and perifollicular localization of hemopoietic foci persists in many cases *during the last months This indicates* an unquestionable correlation with the polyblasts of Maximov and Danchakova which Marchand identifies with undifferentiated perithelial mesenchymatous *cells* of perivascular and perifollicular localization of the hemopoietic foci

The lymphoblastic and lymphocytic diffuse and mixed masses found during the last *2 months of gestation* and more compact masses in the inguinal region suggest the postembryonal genesis of follicular formations in lymphopoietic organs i e., *their appearance* after cutaneous hemopoietic function

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their effect was exam ned after an exposure of 22 24 hours. Of the fatty acid as well as of the alkyl sulfate compounds, those with 12 carbon atoms led most often to erythematous and esicular skin reactions These compounds were followed in their irritating effect by those conta ning 14 and 10 carbon toms respect vely In the same oncentration, the alkyl ulfates were more irritating than the sodium soaps.

It is suggested that the irritating effect is due to direct cellular damage by the anions freed through hydrolysis

Studies on Cholesterol and Cholesterol Esters in Skin Sur face Fats. Dorothy B \\ ndhorst and Roscoe C Foster Jr (Un of Chicago) describe a method by which free and es terified sterol fractions of surface fats were separated by column chromatography and the st rol content in both por tions estimated by the Liebermann Burchard color reac tion The method was applied to scalp and glabrous skin lipids obta ned from normal adults.

In the scalp urface fats and total and free sterols had the lowest concentration n balding men and the highest concen tration in women with nonbalding men occupying an inter mediate position \o such trend was present in fat from glabrous skin The e terified portion of the sterols repre sented a fai ly constant part of the total fat n all samples both from the scalp nd glabrous skin.

The lipid film f the kin surface deri es f om the keratin-izing epidermis and sebaceou glands Most cholesterol stem from the keratinizing ep dermis Thus the concentration of holesterol n an ether extract of th skin surface expresses the relative rate of production of both sebum and keratinized cells That bald g men ha e less total sterols in scalp fat as compared to nonbalding men and t women may mean imply that they ha e an increase in sebaceous gland secre tions which is poor n cholesterol or con ersely they may ha e a relat dec ease in epidermal contribution. The lat ter possibility r lat e decrease in keratinization attrac tive mce baldi g scalps uni ersally show a decrease in one form of kerati zation—hair formation

Since the esterified portion of the total sterols is present in elatively on ta t amounts in the scalp surface fat of ll persons and in l p d from nonhairy skin the esterification mechanism of sterols n skin surface lipids is apparently con

( ) J Invest Dermat 29 339 344, November 957

tosterone propionate under various test conditions Also studied was whether the hair cycle could be started with use of *testosterone propionate* The steroid given daily intramuscularly in doses of 80 mg/kg body weight led to distinct hyperplasia of the epidermis which set in early and *lasted up to 27 days.* There was no relation between the hyperplasia of the epidermis and the hair cycle. The hair cycle could not be started by a 7 or 14-day treatment with testosterone propionate.

White petrolatum applied at different times and with varying frequency to the rat epidermis after it was made hyperplastic by testosterone propionate, caused no essential changes. When colchicine was applied, the epidermis made hyperplastic by testosterone propionate showed great increase in mitoses (Dustin reaction) In a control test Chinon-ethylen imin (Bayer) a cytostatic agent, suppressed hyperplasia of the epidermis after testosterone propionate or petrolatum.

Studies on Irritating Effect of Fatty Acids and Alkyl Sulfates of Certain Chain Length on Human Skin were conducted by K H Schulz and G Rose[1] (Univ of Hamburg Eppendorf) Every washing procedure disturbs the physiologic structure of the surface and the superficial layers of the skin The effect of soaps and detergents depends on their composition length of action concentration and pH values and consists of fat removal roughening shifting the pH concentration of the skin surface and of epidermal swelling These changes are reversible within a few hours. However persistent clinical changes leading to so-called detergent eczema may also develop especially after prolonged exposure

The irritating effect of detergents is certainly not due to their alkalinity only but depends also on their fatty acid and alkyl sulfate content Experience has shown that fats and soaps with a relatively heavy content of fatty acids with a chain length of 10-14 carbon atoms are not so well tolerated by the skin as those *containing fatty acids with 16-18 carbon* atoms.

Sodium salts of saturated fatty acids and alkyl sulfates with an even number of carbon atoms of C_6-C_{18} were tested in watery solution of 0 1 and 0.25% The solutions were applied in small plastic caps directly to the skin and

(1) Arch. klin. u. exper Dermat. 205:254-260, 1957

ficient radiation could penetrate through the stratum corneum into the lower layers of the epidermis to effect con ersion of pro tamin The vitamin so formed could then be eadily absorbed into the blood stream Though the presence of provitamin D in the skin is thought to be related only to formation of vitamin D t is possible that 7-dehydrocholesterol may play a further role in skin metabolism, possibly in the process of keratinization.

► [At recent meeting Wheatley exhibited evidence showing that the skin of patient th psoriasis contains sterol which thus far has not been found in normal skin —Eds]

Determination of Layer Thickness of Commonly Used External Medications to Skin was undertaken by H Ippen and H Betzler[6] (Med. Academy of Dusseldorf) The thicknes f ointment layers may be important in studying resorptiv co d tions o calculating possible toxic effects from drugs applied t the kin The effective concentration of disinfectant, antimycotic o anesthetic pplications depends on the amount del ered to the skin. The layer thickness and ts poss bl v riations ha their greatest importance in the field of skin protecti e preparations and especially in relation to light protecti e agent Thei ability to absorb visible radiation closely related to the thickness in which they re pplied and size of the area covered.

The thicknes f commonly used o ntment bases was determined after their appl cation to ariou areas of the skin Hairy areas were a oided The thickness was calculated from the amou t f radiation derived from a radioacti e I[131]-contam ng compound which was added to the base material The th knes did not depend o the km a ea but ther on th method f application and type of base material The mean al es f thicknes for different materials in microns wer petr lat m 4-10 glycerin cream, 9-15 eu cerin w th water 2-(paraffi o l 3-6 and 10% solution of sopropylmyri t sopropylalcohol, 0.25-1 5

The erage thicknes f se eral base materials when applied to th k aried between 5 and 10 μ. However the minimal alues found ar ften ubstantially below the median alues Th means that the concentration of active ingredients in ki protecti o ntments should be ufficiently high t assure protection en when applied sparingly

► [The layer thickness of the ehicle and concentration of the "active

6) wh Hau erper Dermat 205 221 330, 57

trolled by a system which operates independently of local factors particularly of male-pattern balding Except for the esterified portion the sterols derived from glabrous skin do not follow the pattern of those of the scalp The differences in the free and total sterols in scalp fat observed between balding and nonbalding persons must therefore be a true reflection of local change

Age is an important factor The oldest subjects in any subgroup had the lowest total and free sterol values in fat from the scalp If this trend is primarily evidence for aging rather than for balding then younger balding males show a sign of premature aging in this respect

Presence of Vitamin D Precursors in Human Epidermis. Victor R. Wheatley and Richard P Reinertson[5] (Univ of Chicago) with the technical assistance of David Sher examined separated epidermis dermis and subcutaneous fat for total lipids 7-dehydrocholesterol (provitamin D_3) cholesterol and cholesterol esters Dried samples of epidermis contained 8 4-16% lipid Epidermal lipids contained, on the average 12 times as much provitamin as did the dermal lipid In epidermal lipids 7-dehydrocholesterol accounted for an average of 3.7% of the total sterols compared to 1 6% for dermal lipids Subcutaneous fat contained an average of 0.23% total sterols of which an average of 1 9% appeared to be 7-dehydrocholesterol

The findings indicate that human epidermis contains appreciable amounts of provitamin D The amount present is so high that if it were quantitatively converted to the vitamin about 3 sq in epidermis would give the human daily requirement of the vitamin (400 I U) The exact location of the provitamin in the epidermis is uncertain but it is no longer necessary to postulate that the conversion of the provitamin takes place on the skin surface Others have shown that though radiation of 280 mμ is in t effective in curing ricket in rats that of 297 mμ is 80% as effective Sunlight after atmospheric filtration contains little radiation at 280 mμ, the usual limit being taken as 290 mμ It has been calculated that at 297 mμ 1/56 of the incident radiation will penetrate 0 1 mm epidermis and 1/3 000 penetrates 0 2 mm The thickness of the stratum corneum has been calculated a 0 04-0 05 mm and of the whole epidermis a 0 07-0 17 mm Thus

(5) J Invest. Dermat. 31 51 54 July 1958.

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ingredient obviously are of decisive importance in the case of protective ointments, creams and lotions. As far as topical treatment of skin lesions is concerned, however, the layer thickness seems to have relatively little importance beyond a certain point, except as it may shield and protect the treated area against extraneous effects, such as friction, changes in temperature, air currents, etc.—Eds.]

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